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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY NOVEMBER 6 1948

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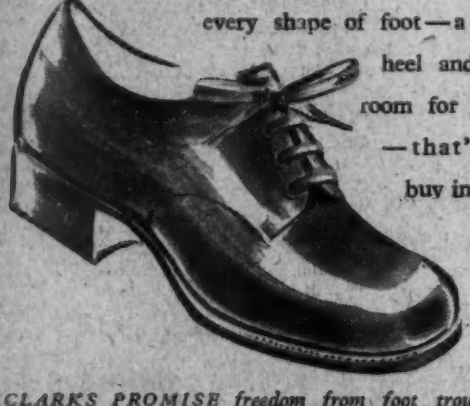

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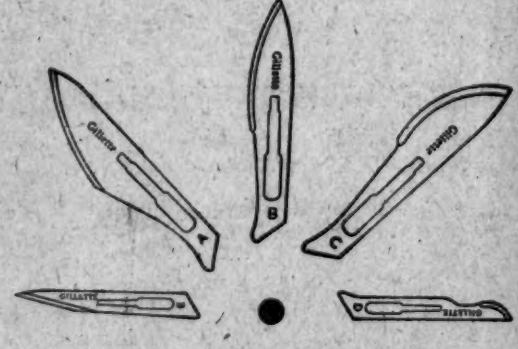

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 6 1948

ETHINYL OESTRADIOL

BY

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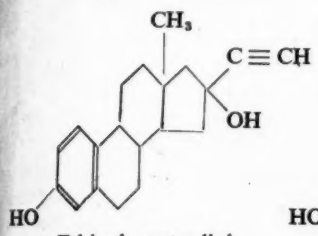
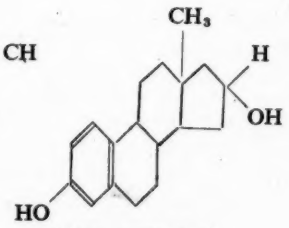
Ethinyl oestradiol is an orally active oestrogen first prepared by Inhoffen and Hohlweg (1938). It is a derivative of alpha oestradiol, the chemical structure of the two substances being very similar.



Ethinyl oestradiol



Alpha oestradiol

It has already received quite an extensive clinical trial, particularly in the U.S.A., but has not been available in this country until this year. Reports on its biological actions and therapeutic value have been published by Clauberg and Üstün (1938), Salmon and others (1941), Groper and Biskind (1942), Soule (1942, 1943), Watson (1942), Lyon (1944), Allen (1944), Harding (1944), Bickers (1946), Wiesbader and Filler (1946), and Birnberg and others (1947). These deal with its effects in women, and indicate that ethinyl oestradiol behaves like other oestrogens in its effect on the female genital tract and breasts, including relief of climacteric symptoms and suppression of lactation. Other reports, such as those by Lawrence and Werthessen (1942), Kearns (1942), Huggins and McDonald (1945), and McCrea (1946), go to show that ethinyl oestradiol also has the expected effect on conditions in the male such as carcinoma of the prostate and haemospermia.

Ethinyl oestradiol has reached this country with an already established reputation for being an effective oestrogen and, moreover, one which even when administered orally is extremely potent. Estimates of its activity vary considerably, but all observers agree that it is the most potent oestrogen so far discovered. Inhoffen and Hohlweg (1938) reported it to be 15 to 20 times as powerful as alpha oestradiol when both are administered by mouth. Harding (1944) found it at least 15 to 30 times, and Soule (1942) 50 to 70 times, as active as alpha oestradiol. Allen (1944) estimated it to be 26 times as active as hexoestrol. Soule (1943) said it is 5 to 20 times as powerful as stilboestrol, but Harding (1944), like Allen (1944), puts this figure at 5 or 6. Most of these estimates appear to be based on its capacity for relieving menopausal symptoms, but Bickers (1946) concluded that in the treatment of anovular uterine haemorrhage 0.3 mg. of ethinyl oestradiol is equivalent to 5 mg. of stilboestrol.

When advance supplies of ethinyl oestradiol were put at our disposal* it was decided to undertake a clinical trial, partly to confirm its value as an oestrogenic agent but mainly to assess its potency. For this purpose inhibition or suppression of lactation was chosen as the test object as it seemed preferable to the relief of climacteric manifestations, where the interplay of psychogenic factors makes the assessment of results difficult. An attempt was made to compare the potency of ethinyl oestradiol and stilboestrol, both being administered orally, and to determine within practical limits the minimal dose of each which is required to inhibit lactation. This latter is extremely difficult, if not impossible, to do with any degree of accuracy, because it varies with the spacing of doses and the number of days over which it is administered and the susceptibility of individual patients. For the purpose of this investigation the usual procedure consisted in starting treatment within twenty-four hours of delivery and in giving gradually decreasing amounts of oestrogen over the course of seven days. In a few of the later cases the duration of treatment was reduced. With a few exceptions the patients were observed for ten to fourteen days only, so any very late relapse will not have been recorded unless it was specially reported by the patient. No other treatment such as saline aperients and restriction of fluid intake was given. The results are classified into:

Excellent.—No sign of breast activity at all.

Good.—Not more than slight secretion or slight fullness of the breasts for one or two days. No discomfort.

Fair.—Moderate secretion or fullness without gross engorgement and insufficient to cause the patient more than minimal discomfort.

Poor.—Varying degrees of engorgement or free secretion of milk, sometimes necessitating a further course of oestrogen therapy.

This type of assessment is similar to but not identical with the one used by Birnberg and others (1947).

Trials with Ethinyl Oestradiol

Ethinyl oestradiol is supplied in tablets, each containing 0.05 mg. active substance, for oral administration. The schemes of dosage employed and the results are set out below. Treatment was started within twenty-four hours of delivery, except when otherwise stated.

Scheme 1.—Technique : 5 tablets b.d. first day, 4 b.d. second day, 3 b.d. third day, 2 b.d. fourth day, 1 b.d. on each of the fifth, sixth, and seventh days of treatment; total, 34 tablets

*We are indebted to Dr. W. J. Tindall, of Organon Laboratories, for a liberal supply of ethinyl oestradiol.

(1.7 mg.). *Results* : Eleven patients treated; ten did not have any sign of breast activity, while the other one noticed slight secretion on the tenth day. (10 excellent, 1 good.)

Scheme II.—Technique : 4 tablets b.d. first day, 3 b.d. second day, 2 b.d. third day, 1 b.d. on the fourth, fifth, sixth, and seventh days of treatment; total, 26 tablets (1.3 mg.). *Results* : Eleven patients treated, nine with excellent result; the tenth had a little fullness and minimal discomfort in the breasts on the fifth day, while the remaining one, a girl of 14, had no breast activity whilst in hospital but is reported to have developed severe pain in the breasts on the fourteenth day, the condition developing into a breast abscess which had to be drained. Not having seen the patient at the time, we are unable to say whether she suffered engorgement of the breasts or whether the condition was an acute mastitis from the time of onset of the symptoms. This case is recorded, however, as showing a poor result. (9 excellent, 1 good, 1 poor.)

Scheme III.—Technique : 2 tablets b.d. first and second days, 1 tablet b.d. third and fourth days, 1 tablet daily on the fifth, sixth, and seventh days of treatment; total, 15 tablets (0.75 mg.). *Results* : (*a*) Eight cases; excellent result in all. (*b*) A second group of seven patients whose babies died after birth were treated by this technique, starting later than the first day after delivery, often when lactation was already established. The results in this series were as follows :

Case	Treatment Started	Result
1	4th day of puerperium	Excellent
2	5th " "	"
3	3rd " "	"
4	2nd " "	"
5	3rd " "	"
6	3rd " "	Poor
7	3rd " "	Excellent

Scheme IV.—Technique : 1 tablet b.d. for first four days, and 1 tablet daily on the fifth, sixth, and seventh days of treatment; total, 11 tablets (0.55 mg.). *Results* : Nineteen patients treated. Excellent result in 14 cases (4 patients not observed personally after the fourth day); good result in 2 cases (1 patient not observed personally after the seventh day); fair result in 2 cases; poor result in 1 case.

Scheme V.—Technique : 1 tablet b.d. for four days; total, 8 tablets (0.4 mg.). *Results* : Two patients treated, both with excellent result.

Scheme VI.—Technique : 2 tablets b.d. on first and third days only; total, 8 tablets (0.4 mg.). *Results* : Two patients treated; one excellent and one fair result.

Scheme VII.—Technique : 1 tablet daily for four days; total 4 tablets (0.2 mg.). *Results* : Three patients treated; two good and one fair result.

Scheme VIII.—Technique : 1 tablet daily on first and third days only; total, 4 tablets (0.2 mg.). *Results* : Three patients treated; one good and two poor results.

From our observations on the treatment of the whole series of 66 patients it is clear that ethinyl oestradiol, as judged by its ability to inhibit or suppress lactation, is an extremely powerful oestrogen. If it is administered orally in divided doses, in gradually decreasing amounts, over the course of seven days, a total of 0.75 to 1.3 mg. is sufficient to ensure good results in a high proportion of cases, if not all. A total of 1.7 mg. produces consistently good results and is probably an unnecessarily high dose. The response was excellent or good in 29 out of 30 women who received 0.75 mg. or more and when the treatment was begun within twenty-four hours of delivery. Nevertheless, judging by the general experience with other oestrogens, it is almost certain that if the number of patients had been larger there would have been included a few who were less susceptible and an occasional poor result would have been recorded. When the dose is reduced to 0.55 mg. a critical level is reached and the treatment may fail or be only partially successful in preventing breast activity. Even so, in a few patients as little as 0.2 mg. appeared to be effective. So far as we can find, the only other workers who have published detailed results on the ability of ethinyl oestradiol to suppress lactation are Birnberg and others (1947). They gave 1.5 mg. over the course of nine days and noted 74% excellent or good results, 16% fair results, and 10% failures among 145 cases.

Trials with Stilboestrol

It is probably true to say that during the last ten years, and in this country, stilboestrol has been the oestrogen most widely used for suppression of lactation. Various techniques are said to give good results. There is no need to review the literature in full, for this was done by Barnes (1942) and Prescott and Basden (1944). Some writers (Diddle, 1941; Gavioli, 1944) claim good results with a single dose of 5 or 10 mg. on the first day; others have been disappointed with the results of giving 35 mg. Some give as much as 45 mg. daily. There seems to be a wide variation not only in the response of individual patients but in the interpretation of results by different observers. Barnes (1942) gave a seven-day course of decreasing amounts of stilboestrol to 81 patients, the total dose being 30 mg. in most cases, but more than this (up to 50 mg.) in 22 cases. The treatment was not completely successful in 32, although in several of these cases there were signs of only minor breast activity. A repeat course of treatment was necessary in 20 patients in all, but these included only one of the 22 who received a maximum dose. This rather suggests that 30 mg. is barely sufficient to ensure the optimum results, for which 40 to 50 mg. is necessary. This conclusion is probably in keeping with the general experience; for most clinicians, despite minor variations in technique, seem to give about this amount over four to ten days and are satisfied with the result. It is also borne out by other writers. Diddle, Nagyfy, and Sells (1942) obtained uniformly satisfactory results using 40 to 50 mg., but noted 4.5% failures when the total dose was between 25 and 35 mg. and 40% failures with 10 to 20 mg. Coulton (1947), while controlling a series of cases treated with "meprane," gave stilboestrol to 73 patients and noted 40% failures when the total dose was between 10 and 20 mg., 4.5% failures when he gave 25 to 35 mg., and no failures with 40 to 50 mg.

For several years now we have as a routine given 41 mg. over the course of eight days, the daily dose being 10, 10, 6, 5, 4, 3, 2, 1 mg., and the results on the whole have been good, although, in common with most observers, we have met occasional failures for which a further course of treatment has been necessary; and even that has sometimes failed. As part of this inquiry it was decided to determine the effects of stilboestrol given in smaller doses. The clinical work of the department is carried out in two hospitals; ethinyl oestradiol was used for all patients in whom it was indicated in one hospital, and stilboestrol in the other. Both groups of patients were unselected, but the observers were not always the same: this latter disadvantage was counteracted as much as possible by having the details of all the results analysed by an independent worker. The details for the stilboestrol therapy are set out below, treatment being started within twenty-four hours of delivery in all cases.

Scheme IX.—Technique : Consecutive daily doses of 5, 4, 3, 2, 1, 1 mg.; total, 17 mg. *Results* : Twenty-two patients treated. Excellent result in 2 cases; good result in 6 cases; fair result in 6 cases; poor result in 8 cases (supplementary course of treatment given in four).

Scheme X.—Technique : Consecutive daily doses of 10, 10, 5, 4, 3, 2, 1 mg.; total, 35 mg. *Results* : Twelve patients treated. Excellent result in 2 cases; good result in 6 cases; fair result in 2 cases (both had a supplementary course of treatment, although it was not strictly necessary); poor result in 2 cases (supplementary course of treatment given in both).

The second group is very small and the significance of the results is doubtful. The findings in both groups are, however, in keeping with those of other writers, and go to show that a total of 35 mg. or less of stilboestrol is hardly enough to ensure consistently good results, while considerably smaller doses are quite unreliable in their effects.

Relative Potency of Ethinyl Oestradiol and Stilboestrol

So far as the suppression of lactation is concerned, and when both substances are given orally in divided doses for seven days, our findings in admittedly small groups of patients lead us to conclude that 0.55 mg. of ethinyl oestradiol is rather more effective than 35 mg. of stilboestrol. A total of 0.75 mg. to 1.3 mg. gives as good if not better results than we have obtained using 41 mg. of stilboestrol as a routine during several years. As judged by its ability to suppress breast activity in the puerperium, ethinyl oestradiol, weight for weight, seems to be not less than 50, and it may be 70, times as potent as stilboestrol. This estimate is higher than that of other workers who based their conclusions on the treatment of menopausal symptoms. It is of course impossible to be exact in these matters because so many factors, such as the rate of absorption, inactivation, and excretion, enter the picture and may act to the advantage of one preparation when one condition is under treatment and to its disadvantage when put to another use. Stilboestrol, for instance, is utilized and excreted quite rapidly. Its fleeting action may be a disadvantage in the suppression of lactation and may explain why late relapse (i.e., breasts filling and secreting on the ninth or tenth day) is relatively common. Our impression is that cases treated with ethinyl oestradiol are less likely to suffer these late relapses, although they do occur. In this respect the suggestion quoted by Lyon (1944) that ethinyl oestradiol is absorbed and utilized comparatively slowly may be significant. Nevertheless this idea is not supported in any strong degree by Lyon's observation to the effect that menopausal symptoms recurred within one to twelve days (average 5.5 days) of suspending treatment. It was the possibility of ethinyl oestradiol having a prolonged action which prompted the treatment of a few cases by Schemes V, VI, VII, and VIII. The results, however, are inconclusive, and further tests with a few doses widely spaced are being carried out.

It was pointed out earlier that several workers have compared the potency of ethinyl oestradiol with that of alpha oestradiol and have variously estimated it to be 15 to 70 times greater. We have no experience of alpha oestradiol, but Diddle and others (1942) reported that for the purpose of suppressing lactation stilboestrol by mouth and alpha oestradiol in propylene glycol administered sublingually are about equal in effectiveness provided the latter is given at regular and short intervals. If this is so then the comparisons made between ethinyl oestradiol and alpha oestradiol can perhaps be taken to give an approximate indication of the relative potencies of ethinyl oestradiol and stilboestrol.

Toxic Effects of Ethinyl Oestradiol

All writers note that ethinyl oestradiol, like most oestrogens and particularly the synthetic ones, is apt to produce untoward symptoms in non-pregnant women. These include nausea, vomiting, headache and malaise, dizziness, and urticaria. Such symptoms are common and occur in about 10 to 15% of cases when the daily dose is 0.1 to 0.15 mg., and in 20 to 25% when doses of the order of 0.3 mg. daily are given (Harding, 1944; Lyon, 1944; Birnberg, 1947). Reduction of the dose results in disappearance of the toxic manifestations. It would appear that most non-pregnant women can take 0.05 mg. a day without ill effect, although even this small dose may cause nausea and vomiting in some (Birnberg, 1947). These observations are of interest because it has often been stated that it is the synthetic oestrogens which produce vomiting and that the natural ones do not: ethinyl oestradiol is a derivative of the naturally occurring oestradiol, and yet is as liable as, if not more liable than, synthetic oestrogens to cause nausea and vomiting. They rather favour the view which has long been taken by some workers, that the toxicity of any preparation, natural or synthetic, is dependent on its oestrogenic activity rather than its chemical structure. In our clinical trial no ill effects of any kind were noted.* This is not surprising, because pregnant or recently pregnant women rarely show toxic reactions even when given massive doses of any form of oestrogen. Thus it is well known that as much as 1,000 to 2,000 mg. of stilboestrol can be given within four to seven days without upsetting a puerperal woman. We have confirmed this to the extent of giving 700 mg. in seven days to three patients.

Now that ethinyl oestradiol is becoming freely available in this country it is perhaps relevant to point out that, like other oestrogens, it may have other undesirable side-effects, and the likelihood of these again reflects its high potency. For instance, even in moderate doses it can cause endometrial proliferation to the state of hyperplasia (Wiesbader and Filler, 1946; Birnberg and others, 1947), with resulting heavy uterine losses and a disturbed menstrual cycle (Harding, 1944). Soule (1943) reported that as little as 0.85 mg. given in divided doses can cause uterine haemorrhage in a post-menopausal woman, and Birnberg and others (1947) noted that 20% of women given 0.05 to 0.15 mg. daily for climacteric symptoms developed post-menopausal haemorrhage. In women who are still menstruating 0.05 mg. daily sometimes delays the onset of menstruation or makes the menstrual flow excessive (Lyon, 1944). Also, like other potent oestrogens, ethinyl oestradiol is liable to cause swollen and painful breasts and to lead to deep pigmentation of the nipple and areola. If, therefore, its use becomes widespread—and it is likely to, for the drug is cheap and efficient and can be given by the oral route—the fact that it is extremely potent should be recognized, otherwise it will almost certainly be the cause of many cases of post-menopausal haemorrhage in older women and menstrual disturbances in younger ones. Since 0.05 mg. is equivalent to not less than 1 mg. of stilboestrol and may well be equal to 2 or 3 mg., it is probably too powerful a preparation to use for the relief of climacteric symptoms. The introduction of tablets of weaker strength might obviate this difficulty.

Summary

An account is given of a clinical trial of ethinyl oestradiol—an oestrogen new to this country.

Its ability to suppress lactation in a series of 66 patients is assessed and compared with that of stilboestrol. The results go to show that ethinyl oestradiol is most efficient in preventing activity of the breasts.

A total dose of 0.75 to 1.3 mg. spread over seven days gave good results in 21 out of 22 cases. When the total dose was reduced to 0.55 mg. the results were less satisfactory but rather better than those obtained with 35 mg. of stilboestrol. Since it takes 40 to 50 mg. of stilboestrol to produce good results in a high proportion of cases it is reckoned that ethinyl oestradiol is at least fifty times more active than stilboestrol for the purpose of suppressing lactation.

There is evidence in the literature that it is equally potent in producing other oestrogenic effects; thus when it comes

*Since completing this series of cases we have seen one puerperal woman develop an urticarial rash twenty-four hours after taking 0.55 mg. of ethinyl oestradiol within the space of twelve hours. The rash may or may not have been caused by the drug.

into general use there will be need for caution over dosage, otherwise ill effects such as menstrual disturbances, endometrial hyperplasia, and post-menopausal bleeding, as well as toxic reactions such as nausea and vomiting, will be commonly seen.

We are grateful to the other members of the medical staff of the Liverpool Maternity Hospital and Mill Road Infirmary for allowing us to carry out this trial on their cases.

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MÉNIÈRE'S SYNDROME

SUCCESSFUL TREATMENT BY SURGERY ON THE SYMPATHETIC

BY

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Ménière first described his syndrome in 1861, but had inadequate knowledge of the underlying aetiology. He reported a case of a patient who died after an acute illness of five days, and described the necropsy findings; it would seem that acute haemorrhagic labyrinthitis was the cause of the syndrome.

By definition Ménière's syndrome is a malady characterized by attacks of rotational vertigo accompanied by a tendency to fall, occurring at irregular intervals and associated with tinnitus and progressive nerve deafness. The attacks are sudden in onset and may occur without warning, and if severe the patient may fall to the ground with great violence. Commonly there is an associated vomiting, which may be of varying severity, sometimes lasting for hours to the point of exhaustion. Accompanying these vestibular disturbances are degrees of cochlear involvement the symptoms of which are tinnitus and nerve deafness. At first the nerve deafness is mild and occurs only with the attacks, but in the later stages of the syndrome it becomes progressively worse and is manifest permanently between the attacks, until finally it is complete on the side affected.

In the earlier stages the patient is free from giddiness between the attacks, but with progression of the syndrome there is a constant state of dizziness, which is considerably accentuated by any sudden movement of the head.

The tinnitus is variable in type and severity; it may be a pulsating throbbing variety or a high-pitched constant note either singing or hissing in character. There is no known precipitating factor, and the absence of premonitory signs makes the attacks the more distressing, the patient developing a constant dread of the next occurrence; thus a not inconsiderable functional element quite often exists with the syndrome—a fact recorded by Levy, O'Leary, and Furstenberg—and great care has to be paid to detail in the examination in order to determine the degrees of organic and functional symptoms.

Aetiology

Much confusion exists about the exact aetiology of Ménière's syndrome, as evidenced by the considerable volume of literature on the subject and the extreme diversity of views expressed—some substantiated by necropsy findings and pathological investigations, some based purely on clinical observation and empirical therapy, and others founded very largely on assumption. Attributable factors in the literature cover such a wide field as poisoning from lead, mercury, arsenic in alcohol, drugs such as salicylates, circulatory disturbances of hypertension, arteriosclerosis, anaemia, the exanthemata, the chronic infections, syphilis and tuberculosis, virus infections, chronic diseases such as leukaemia, purpura, and pernicious anaemia, tumours of the cerebello-pontine angle, and trauma.

Causative theories are equally diverse, ranging from disturbance of sodium metabolism in the local tissues (Furstenberg) to vascular disturbances. The latter Miles Atkinson describes as the "mechanics" of Ménière's syndrome, and the patients are divided into two groups determined by an intradermal histamine test—a vasoconstrictor group and a vasodilator group, in the ratio of five to one. He then treats them accordingly with nicotinic acid or histamine.

Hallpike and Cairns noted at necropsy a distension of the endolymphatic system, with degenerative changes in the organ.

Anatomical Consideration

The blood supply of the inner ear is derived from two sources. The first, of major significance, is the internal auditory artery, which, as is common knowledge, is a branch of the anterior inferior cerebellar artery; or, less commonly, it may arise direct from the lower part of the basilar artery. This in turn is formed by the union of the vertebral arteries at the base of the skull.

The subsequent course of the internal auditory artery is through the internal auditory meatus, accompanying the auditory and facial nerves to its distribution near the inner ear. This distribution would seem to take various forms according to Nabeya, ranging from an almost equal dichotomous division into cochlear and vestibular arteries to a predominant cochlear artery with smaller branches to the vestibule and vice versa, or a vestibular artery dividing to send branches to both cochlear and vestibule. Siebenmann describes the blood supply as a more or less equal division of the internal auditory artery to both cochlear and vestibular fields of distribution. It would seem that the variability of the distribution of the arteries indicated by Nabeya might well account for the variable degree of association of cochlear and vestibular signs in Ménière's syndrome-complex. This would reasonably fit in with the view held by us that the predominant aetiological factor is one of vasoconstriction, and that the smaller vascular distribution to a particular portion of the organ will imbue

that artery, by virtue of its size, with greater vasoconstrictor properties—hence a preponderance of symptomatology of the organ of distribution.

The second source of blood supply to the inner ear arises from vessels of the middle ear. This is said, however, to be a somewhat rare source, and need hardly be considered as presenting a possible fallacy in the rationale of treatment.

Bergglas found around such vessels as the iliac arteries large nerve strands at the union of the adventitial and muscular coats. He believed that this plexus extended throughout the muscular tree and was everywhere continuous.

H. H. Woollard states that vascular tone from the aorta to the periphery is maintained by vasomotor nerves in two ways. First, in the aorta large bundles from adjacent sympathetic ganglia composed almost entirely of non-medullated nerve fibres pass into the adventitia, some lying superficial and some deep near the media. The bundles continue to the periphery, forming a plexus of non-medullated fibres from which further fibres pass inwards and form an abundant mesh of the finest fibres within the muscle coat. Secondly, from the peripheral nerves these fibres are almost entirely medullated. The muscular coat is innervated by the fine network, the individual elements of which divide and fuse together to give absolute continuity complete throughout the vascular wall. Physiologically, Langley, Bayliss, and Gaskell have shown that bars of constrictor fibres are exclusively sympathetic ganglionic and that there is no other source of supply.

Hence destruction of the cell station in the stellate ganglion and blocking of the post-ganglionic pathways to the auditory vessels would presumably deal with the problem if the vasoconstriction is of central origin, for it is yet to be seen whether sensitization of sympathetic nerve endings to adrenaline or adrenaline-like bodies occurs in the terminal branches of the internal auditory artery after removal of the stellate ganglion. This destruction is undertaken by ganglionectomy and stripping and cutting the vertebral artery. It was felt that cutting the artery was necessary because of the possibility of impulses being conveyed through the intramural plexuses, a number of which exist, as shown by H. H. Woollard, at varying depths in the arterial wall. Also Leriche's periarterial sympathectomies never proved effective, the spasm returning to the vessels from days to weeks after the operation, hence indicating the probable existence of alternative pathways. Woollard showed that the nerve supply of arteries came from two sources—the one from periarterial fibres, and the other from neighbouring nerves. The fibres from neighbouring nerves were myelinated and probably not of vasoconstrictor function, so that the failure of Leriche's operation would seem to be due to the establishment of the pathway again, probably through the arterial wall itself.

That after ganglionectomy and cutting of the artery there is the possibility of sympathetic impulses reaching the vessel from the opposite vertebral artery via the circle of Willis, or alternatively from the component of Oort of the eighth nerve, has not been overlooked, but to the best of our knowledge no evidence in support of these sources is known. It is conceivable that primary nerve deafness may also be due to vasoconstriction, since the deafness is part of the syndrome, the possibility in these cases being that the effect of the spasm is felt by the artery of supply to the eighth nerve, with subsequent permanent damage. It was with this in view that a few cases of early pure nerve deafness were selected for operation, and research in this field is being continued.

In the absence of definite pathological evidence it would seem that vasoconstriction plays a predominant part in the production of the syndrome. Siebenmann points out that the internal auditory artery which supplies the labyrinth may be readily influenced by excitation of the vasoconstrictors on account of the narrowness of the artery relative to the basilar artery. Its state of contraction depends upon the nerve plexus surrounding the vertebral artery and its branches coming from the thoracic part of the sympathetic cord and inferior cervical ganglion. It was with this in view that a means to prevent the flow of impulses through the plexus was attempted.

The Operation

Under intratracheal gas-oxygen with positive pressure the anterior approach is favoured, with the patient in a supine position and the head extended and rotated to the opposite side. This serves to bring the transverse process of the seventh cervical vertebra into prominence. Through a 2-in. (5-cm.) slightly curved incision dissection of the subclavian triangle is carried out down to the deep fascia of the neck. The clavicular head of the sternocleidomastoid muscle is divided ½ in. (1.25 cm.) above its clavicular origin. The phrenic nerve is then isolated and retracted out of the way. The scalenus muscle is divided and the second part of the subclavian artery is then seen. Careful dissection brings into view the thyroid axis, and if the dissection is carried anteriorly the vertebral artery is exposed. It is sometimes a help to divide the inferior thyroid artery between ligatures. When this is done the vertebral artery becomes more accessible, and its adventitious coat may then be stripped from the origin of the artery until it enters the foramen in the transverse process of the sixth cervical vertebra. This artery is larger than one might expect, often being twice the diameter of the inferior thyroid artery. It arises from the upper and back portion of the subclavian artery, and its exposure may be facilitated by retracting the subclavian artery downwards and forwards. In the areolar tissues surrounding the artery may be found sympathetic branches from the stellate ganglion, which it crosses. The vertebral artery is freed and then divided between ligatures. Careful dissection is made through Sibson's fascia, and the parietal pleura is stripped downwards as far as the transverse process of the second thoracic vertebra. This brings into view the pre-ganglionic fibres of T.1 and T.2 as they ascend to blend with the inferior cervical ganglion to form the stellate ganglion, the variations and branches of which are notorious. This ganglion is freed from its surrounding loose fatty areolar tissue and excised after dividing the pre-ganglionic fibres of T.1 and T.2. Several small veins in this tissue may sometimes cause temporary and troublesome oozing if torn. The wound is then closed in layers. Only six days' stay in hospital is necessary.

Immediate Result of the Operation

Horner's syndrome is of course apparent at once. The contracted pupil and ptosis of the upper eyelid rarely worry the patient after the first few days and tend to correct themselves during the first few months. However, should the ptosis persist a small plastic operation is all that is required to raise it. The dryness of the hand does not cause discomfort.

Ear.—Patients state that the head feels clearer and that they no longer have the sense of uneasiness or feeling of pressure in and around the ear that Ménière's syndrome produces, and the ear loses its stuffed-up feeling. The effect on the tinnitus is varied. In Cases 4, 5, and 9 it was completely relieved, in six cases it was partly alleviated, while in the remaining three it was unaltered. The hearing shows immediate improvement, which has been maintained for the time those cases have been under observation.

It is well known that Ménière's syndrome often affects one ear after the other. We have not yet had the

condition occur in the ear of the unoperated side, but, if it should, then there is no valid reason why the stellate ganglion of that side should not be removed, together with stripping and possible ligation of the vertebral artery, though the safety of this latter procedure should first be proved by animal experimentation. This mode of treatment has been so effective that it suggests the possibility of successfully alleviating an acute attack of Ménière's disease by means of a "novocain" block of the stellate ganglion—a relatively simple procedure.

Nose.—Some dryness of the mucosa is observed, but this is not maintained for more than a few weeks.

Throat.—Nothing observed.

Taste and smell remain unaltered, and there is no appreciable effect on salivation.

Complications.—The disturbance of circulation through the vertebral artery might conceivably give rise to thrombosis of the post-inferior cerebellar artery in arteriosclerotics. This would then result in degenerative changes in the dorso-lateral area of the medulla, probably involving the dorsal and ventral spinocerebellar tracts, the spinal tract and nucleus of V, the lateral spinothalamic tract and nucleus ambiguus, and even the vestibular nerve. However, since the original syndrome may be caused by the arteriosclerosis, operation is not undertaken in these cases, and therefore the complication is hardly likely to occur.

Case Reports

Reports of twelve cases operated on during the last twelve months are given. The routine clinical examinations, including calorie tests and inflation of eustachian tubes, were carried out. Calorie tests showed normal variations that are encountered with labyrinthine dysfunction due to Ménière's syndrome. In all cases the eustachian tubes were patent. Audiometric examination was made of all ears, and records of both air and bone conduction were taken, but for the sake of brevity only air-conduction records are published. Wherever the air conduction was improved there was a corresponding improvement in the bone conduction.

Case 1.—A married woman aged 46 had had severe attacks of giddiness for seven months—she fell four times in one week. Attacks occurred every two or three days, starting with great roaring in the left ear and completely prostrating her for 24 to 48 hours. Severe deafness and tinnitus involved both ears. There was no great improvement on salt-free diet and sedation for three months. There was a history of previous middle-ear disease (right ear), but this had now cleared up.

On July 1, 1947, left stellectomy, with division of preganglionic fibres of T.1 and T.2 and division of fibres going to vertebral artery, was carried out. There was immediate relief of vertigo and tinnitus (pulsating tinnitus completely relieved); though an occasional high-pitched note was present. Hearing was greatly improved for both air and bone conduction.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	60	70	90	90	100	—
" " June 1, 1948 ..	45	45	60	70	65	80

Case 2.—A man aged 25 had a sudden onset of vertigo in December, 1946, accompanied by severe tinnitus in the right ear and vomiting, and was confined to bed for three weeks. Further attacks from January to March, 1947, were accompanied by increasing deafness. He was then free until June, when attacks restarted. Tinnitus had persisted since the first attack, and was of the continuous type. In June, 1947, he was given a salt-free diet, with sedation, restricted fluids, and injection of calcium: no improvement resulted in either giddiness or tinnitus. He had also had migraine since boyhood.

Operation (July 1, 1947): right stellectomy and stripping of vertebral artery. Result: except for a slight attack of giddiness on Sept. 2, accompanied by tinnitus in the left ear, there has been no further attack; the hearing has very much improved and the tinnitus, while still present, has greatly lessened, and he has had no further attack of migraine to date.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	55	60	65	55	75	—
" " June 7, 1948 ..	30	30	25	20	45	65

It is highly probable that the slight attack on Sept. 2 was due to Ménière's syndrome affecting the other ear.

Case 3.—A woman aged 21 underwent a fenestration operation for clinical otosclerosis (by E.R.G.P.) on the left ear on Aug. 20, 1946, with a satisfactory result. On June 16, 1947, she began to complain of an increase in the tinnitus of the right ear, accompanied by severe attacks of vertigo and vomiting. It was decided that the fenestrated ear was not responsible for the syndrome. Cocainization of the spheno-palatine ganglion on the right side completely relieved the tinnitus for several hours.

Right stellectomy was performed on Aug. 14, and next day the head was clear and the noises had ceased. Up to May 29, 1948, no further attacks of giddiness had occurred, but slight tinnitus of a continuous character had returned: the tinnitus could be stopped by biting hard on a piece of cork between the right upper and lower molars. The hearing has decidedly improved.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	35	30	40	35	45	55
" " June 8, 1948 ..	20	20	25	15	35	50

Case 4.—A woman aged 32 had for 10 years had increasing deafness of nerve type, associated with severe tinnitus and bouts of vertigo, the latter symptom being present during the past three years and increasing in frequency and severity. Right stellectomy was performed on Aug. 15, 1947. Up to June 16, 1948, no further attack of vertigo had occurred, and there was complete cessation of tinnitus and great improvement of hearing.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	45	40	55	60	45	40
" " Post-op. ..	35	35	40	40	20	30

Case 5.—A man aged 65 had his left ear first affected in 1946; he had severe giddiness, vomiting, tinnitus, and increasing deafness with each attack. In 1947 the right ear started to be involved, with severe prostrating attacks. Tinnitus of continuous and pulsating types was present for 21 months. There had been no previous middle-ear disease.

On Aug. 29, 1947, right stellectomy, with division of preganglionic fibres of T.1 and T.2 and sympathetic nerves going to vertebral artery, was carried out. On Sept. 1 there was no giddiness, no tinnitus in right ear, and the head felt clear. On March 31, 1948, the giddiness and tinnitus had gone and the hearing was greatly improved for both air and bone conduction.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	35	35	35	40	40	70
" " June 14, 1948 ..	30	20	10	20	40	75

Case 6.—A male fitter aged 48 had a history of 2½ years' severe prostrating attacks of vertigo accompanied by vomiting, deafness, and tinnitus in the left ear. Tinnitus was of a continuous roaring nature. On Jan. 8, 1948, left-sided stellectomy was performed, with stripping of the vertebral artery. On April 22 there was no giddiness; the tinnitus was unaltered, but hearing had somewhat improved.

Cycles per Second:	128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.	40	50	60	65	50	45
" " June 12, 1948 ..	25	35	45	40	35	45

Case 7.—Two years ago a man aged 71 began to have severe attacks of giddiness which, despite all conservative treatment,

including nicotinic acid, continued until he was unwilling to leave the house. Hearing steadily deteriorated in the right ear, and was accompanied by a continuous high-pitched tinnitus, which became worse before an attack. In childhood the patient had had a suppurative otitis media.

On Feb. 2, 1947, right-sided stellectomy was carried out. By Jan. 24, 1948, the attacks had lessened, and he could walk even during an occasional mild feeling of unsteadiness. On Feb. 9 the noises were unaltered, but no attacks of giddiness now occurred. On May 3 he was playing golf for the first time since the onset of vertigo, and now drives his car without any apprehension.

Cycles per Second:		128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.		25	35	45	55	—	—
" " June 11, 1948		35	45	50	55	55	75

This case shows gradual improvement of the high frequencies.

Case 8.—A woman aged 53 had a history of shingles on the left side of the face accompanied by severe attacks of giddiness, which came on usually while she was sitting quietly and was aggravated by stooping. Nerve deafness was present in the left ear. There was tinnitus, both pulsating and continuous.

On Feb. 5, 1948, left stellectomy was done, with stripping of the vertebral artery. On March 2 there was no further vertigo; the head felt clearer, and the left side of the nose, which was always blocked, especially at night, was free. This nasal obstruction was not complained of before the operation, and unfortunately no particular note was made of the condition of the nasal mucosa on the left side, though now it appears less congested than the right side. The tinnitus is unaltered.

Cycles per Second:		128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.		20	25	35	35	45	60
" " May 22, 1948		25	25	30	20	25	50

Case 9.—Six years ago this patient, a woman aged 41, had vertigo on and off for one year, with increasing deafness of the left ear associated with a continuous low buzzing sound. Two years ago vertigo restarted with deafness and tinnitus in the right ear. Rest, salt-free diet, and sedation brought about considerable improvement in the vertigo, deafness, and tinnitus, but symptoms recurred immediately this treatment was stopped. It was considered advisable to try to save the remaining hearing in the right ear, so sympathectomy was decided upon.

On March 15, 1948, right stellectomy was performed, with division of the pre-ganglionic fibres of T.1 and T.2, and stripping and ligation of the vertebral artery. There was an immediate cessation of vertigo and a clearer feeling in the head. Tinnitus had ceased and a great improvement had occurred in air and bone conduction.

Sept. 21, 1948. This patient had a recurrence of her vertigo and unsteadiness accompanied by tinnitus and deafness. The attack was very mild compared with her former attacks, but nevertheless was a definite one.

Cycles per Second:		128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.		35	40	50	50	40	30
" " June 16, 1948		10	20	10	15	15	25

Case 10.—A woman aged 33 had an 18-months history of slowly increasing nerve deafness and tinnitus in the right ear accompanied by bouts of severe vertigo with nausea and vomiting, each attack leaving the hearing worse than before. Right-sided headache and deep mastoid pain of a shooting character were also present. She had undergone conservative treatment for nine months, together with repeated eustachian inflation, without improvement. For a period of five weeks noises were greatly reduced. The patient felt more comfortable, and the sensation of pressure in the region of the right ear had lessened.

Cycles per Second:		128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.		25	35	35	35	20	25
" " June 14, 1948		20	30	35	15	20	30

On April 31, 1948, right stellectomy with division of the vertebral artery was performed. When examined on June 14 there was no further giddiness, and she said her head felt clearer than it had since deafness began. Hearing had improved, but the tinnitus had only slightly lessened.

Case 11.—This patient, a woman aged 63, gave a history of sudden onset of very severe attacks of vertigo accompanied by deafness and tinnitus during the past 16 months. The tinnitus was like faintly escaping steam, and the deafness had been much worse during the last four weeks. She was very apprehensive of further attacks. Sedation and calcium tried over a three-months period gave no relief.

Right stellectomy and ligature of vertebral artery were carried out on May 17, 1948, and by June 14 there was no giddiness whatsoever. She then led a normal active life and did her household work. The head felt clearer, but she complained of slight pain and weakness of the right forearm. This was rapidly lessening. Tinnitus was still present, but was decreasing. The hearing had not appreciably altered.

Cycles per Second:		128	256	512	1,024	2,048	4,096
Loss in decibels: Pre-op.		50	45	45	50	30	60
" " June 14, 1948		50	45	50	50	25	45

Case 12.—In 1934 this patient, aged 38, had her first attack of giddiness, with tinnitus in the left ear. She was free of further attacks until 1946, but they had been present on and off ever since. When attacks were severe they were accompanied by vomiting and an increase in the tinnitus in the right ear. The hearing of the left ear had remained practically stationary since 1934, but that of the right ear steadily decreased with each subsequent attack. As she had a history of three miscarriages a Wassermann test was done, and this proved negative. The tinnitus was worse at the beginning of an attack and faded off altogether for a few hours after the vomiting had ceased. The noises were relieved to a soft murmur by cocainization of the spheno-palatine ganglion of the right side.

On May 14, 1948, right stellectomy with division of vertebral artery was performed. On June 12 there was no giddiness, the tinnitus had lessened, but the deafness had not yet improved.

Pathological examination of the stellate ganglion was carried out in all cases, but no abnormality was discovered in any of them. This finding may be compared with that of J. W. Budd (quoted by Mogan and Baumgartner, 1945), who demonstrated definite pathological changes in the superior cervical ganglion in a case of Ménière's disease, as did J. W. Kernohan, of the Mayo Clinic. Details of the results are given in the accompanying table.

Details of Results

Case No.	Stellate Ganglion	Vertebral Artery	Vertigo	Tinnitus	Hearing
1	Excised	—	Relieved	Lessened	Improved
2	"	Stripped	"	"	"
3	"	—	"	"	"
4	"	—	"	Relieved	"
5	"	—	"	"	"
6	"	Stripped	"	Unaltered	"
7	"	—	"	"	"
8	"	—	"	"	"
9	"	Stripped and ligated	" *	Relieved	"
10	"	"	"	Lessened	"
11	"	"	"	"	Stationary
12	"	"	"	"	"

* See report on Case 9.

Summary and Conclusions

A series of 12 cases of Ménière's syndrome which failed to respond to conservative treatment were subjected by one of us (E.R.G.P.) to stellectomy and division of the pre-ganglionic fibres of thoracic 1 and 2. In two cases the vertebral artery was stripped, while in four cases it was either ligated or divided after the adventitious coat had been removed. The reason for the latter process is given in the context. In each case the vertigo attributable to that ear has been completely relieved except in Case 9.

Whether the recurrence of vertigo in this case was due to hypersensitivity to adrenaline or adrenaline-like bodies following excision of the ganglion (for the patient was hard at work again and under considerable mental strain), or whether some sympathetic fibres to the ear may also originate on the opposite side to a greater or lesser extent in individual cases, is not known, but the fact that there has been a marked improvement on the administration of ergotamine would suggest that the former view is the more likely of the two, in which case division of the pre-ganglionic fibres together with stripping and ligation or division of the vertebral artery would be the operation of choice. This has now been done in more recent cases with the same beneficial result on the vertigo, added to which it has the advantage of avoiding a Horner's syndrome.

The result upon the tinnitus is apparently unpredictable, though on the whole it was reduced—in three cases it was completely relieved. The relief seems to be more pronounced with the pulsating type of tinnitus than with the continuous variety. Each patient suffered from concomitant nerve deafness, and in all except the last two most recent cases there has been improvement (in some ears very markedly) of hearing by both air and bone conduction. If the nerve deafness is very severe it is beyond relief.

It is felt that further work along these lines will greatly aid in elucidating the aetiology and pathology of this distressing complaint and its accompanying tinnitus and nerve deafness.

It is interesting to record that a further series of stellectomies has been performed for tinnitus alone (to be published later), but we forbear to make further comment on the role of the sympathetic on tinnitus at this stage.

In the meantime a new surgical method of treating Ménière's syndrome, having tremendous advantages over the old surgical destruction of the internal ear, is at our disposal.

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For the last two years 45 severely disabled men have been happily and gainfully employed at Haven Products, Ltd., a "sheltered workshop" on Clydeside. They work a regular 8-hour day five days a week and are paid a basic wage of 2s. 1½d. an hour plus bonuses. The Nuffield Provincial Hospitals Trust has recently published an illustrated pamphlet describing the development of the workshop and the work done there. The men manufacture electro-thermic quilts, and the machines are adapted to suit the needs of individual workers. Doors are made specially wide to allow invalid chairs to pass through, lavatories have railings fitted so that men who must use their hands to get about may be helped, and transport is organized from the workers' homes. Four travel to the workshop in motor-chairs and fifteen require ambulance transport. A medical advisory committee, consisting of consultants from the three large voluntary hospitals in Glasgow, a senior medical officer of the Ministry of Pensions, three almoners, and an observer from the Ministry of Labour, was set up to advise on the planning and equipment of the factory, to help in the selection of suitable disabled men, and to ensure that the men's disabilities were not aggravated by their work. The men are medically examined every year, but medical supervision is kept in the background so far as possible. The venture has been very successful both financially and as an experiment in the restoration of the men's self-confidence and contentment. Harmonious relationships prevail in the workshop, and the report emphasizes particularly the enthusiasm and the sense of corporate life enjoyed by the men. Copies may be obtained from the Nuffield Provincial Hospitals Trust, 12 and 13, Mecklenburgh Square, London, W.C.1, and 10, Duke Street, Edinburgh.

"RHEUMATOID DISEASE" WITH JOINT AND PULMONARY MANIFESTATIONS

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It will be generally accepted that rheumatoid arthritis, like pulmonary tuberculosis, is a systemic disease with local manifestations, the former in the joints, the latter in the lungs. Moreover, its systemic nature may be manifested, as recent studies have shown, by widespread pathological changes in various tissues and organs.

Our own studies, confirming those of other observers (see Hench *et al.*, 1948), have shown that in certain cases the bones may exhibit atrophy and even widespread cystic changes, and the peripheral nerves may become involved, with resultant neuritic pains, paraesthesiae, and trophic changes. Biopsy studies of the muscles may reveal microscopic alterations in the form of perivascular lymphocytic infiltration and macrophages in the perimysium and endomysium akin to those sometimes seen in periarteritis nodosa and disseminated lupus. Cardiac lesions may also occur almost identical with those following rheumatic fever, while other accompanying lesions may be found in the spleen, liver, lymph glands, subcutaneous nodules, pleura, and even in the eye in the form of iritis and scleritis. In one recent case there was good reason for regarding a kidney lesion (Ellis type 2) as part of the rheumatoid process.

The purpose of this paper is to report three cases in which an accompanying pulmonary lesion appeared as an integral part of the "rheumatoid state." A careful search of the literature has not disclosed any earlier records.

Case 1

A fitter's mate aged 47 was admitted under the care of one of us (P. E.) to the Rheumatism Unit and later to the Leatherhead Emergency Hospital, and when first seen on Dec. 14, 1945, gave the following history. Two and a half years previously, while he was in a fair state of general health, pain and stiffness started in the right knee-joint. During the next few months the fingers, wrists, elbows, and left knee became involved. Swelling of the affected joints was present while active and subsided with rest. Until the time of admission he had had several courses of physiotherapy at different hospitals. He had lost 2 st. (12.7 kg.) in weight since the onset of the illness. There was a previous history of pleurisy progressing to empyema at 11 years of age, and malaria at 21 and 24 years. There was no significant family history.

On examination he was pale and toxic, and wasting involved subcutaneous tissues and muscles. Examination of the locomotor system revealed evidence of swelling of the proximal interphalangeal joints, wrists, elbows, and knees, and fibrous nodules were present over both olecranon processes, sacrum, and scalp. Examination of the lungs showed poor air entry, and breath sounds diminished at both bases, where numerous crepitant rales could be heard. The heart, abdomen, and central nervous system were normal. Blood pressure 130/90.

Pathological investigations showed: E.S.R., 56 mm. at first hour (Westergren); red cells, 3,670,000. Hb, 66%; C.I., 0.83; white cells, 8,000 (polymorphs 67%, lymphocytes 29%, monocytes 3%, eosinophils 1%); G.C.F.T., negative; serum uric acid 1.2 mg. per 100 ml.; Mantoux, weak positive. Repeated sputum examinations, including concentration techniques, were all negative for tubercle bacilli. General bacteriological examination of the sputum was not significant. Fluid aspirated from the left knee-joint was purulent and contained many polymorphs, but was sterile on culture.

Radiological examination of the wrists, knees, and finger-joints showed osteoporosis, loss of joint space, and erosions characteristic of the rheumatoid type of arthritis. There was evidence of a fine reticulation throughout both lung fields with a chronic bronchopneumonic lesion.

On March 26, 1946, he began to complain of cough and produced small amounts of mucopurulent sputum. In April he developed a generalized purpura, but the bleeding-time was normal and platelets numbered 310,000 per c.mm. His general condition gradually deteriorated, and he became increasingly wasted until June 17, when he developed a pyrexia ranging about 99–100° F. (37.2–37.8° C.), became dyspnoeic and cyanosed, and coughed up much frothy sputum. These symptoms gradually increased in severity, being unaffected by penicillin therapy, until his death on June 23.

Post-mortem Examination (performed by Dr. D. N. Nabarro 18 hours after death).—The body was that of a middle-aged poorly nourished man with polyarthritis. The dura mater was somewhat adherent over the surface of the brain, which was

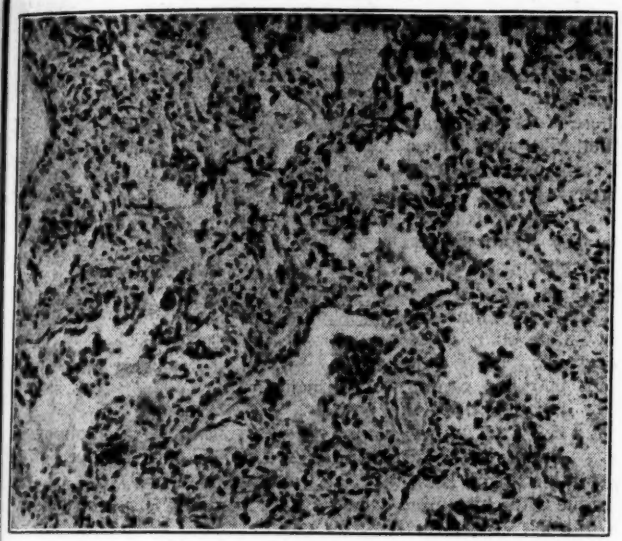

FIG. 1.—Case 1. Photomicrograph showing interstitial pneumonitis with well-marked fibrosis between the lung alveoli. (× 100.)

slightly congested but was otherwise normal. *Respiratory system:* There were fairly dense pleural adhesions, more especially marked over the lower lobes; no free fluid was seen. The trachea and bronchi contained muco-pus. The lungs were firm throughout, with nodular areas suggestive of a bronchopneumonia. Both lungs were congested and oedematous, and on section showed many areas of recent bronchopneumonia. However, the lungs as a whole were firmer than normal and suggested a chronic fibrosing pneumonitis. There was no evidence of tubercle or sarcoidosis. The mediastinal glands were enlarged and showed evidence of chronic inflammation. *Cardiovascular system:*—The pericardium contained some 30 ml. of clear straw-coloured fluid. The heart was dilated and slightly enlarged, and the myocardium was pale, soft, and flabby. The valves were all normal and showed no vegetations or any evidence of endocarditis. There was very little atheroma in the blood vessels. *Gastro-intestinal tract,* normal. The *liver* was somewhat enlarged, appearing firm with a rather coarse mottled surface. There were no gall-stones. The *spleen* was considerably enlarged (weight 630 g.), with a fair amount of perisplenitis. The *kidneys* were not abnormal. The other organs were all normal, and none showed any evidence of tubercle or sarcoidosis.

Histological Report.—Sections were cut of the lungs, lymphatic glands, pancreas, suprarenals, heart, kidney, spleen, liver, and knee-joint and stained haematoxylin and eosin and haematoxylin and Van Gieson. *Lung* (Fig. 1):—The changes chiefly seen were those of an interstitial pneumonitis with a terminal bronchopneumonia, together with the formation of some small abscesses. The alveoli contained considerable exudate; in some the exudate was chiefly albuminous fluid, but in most there was infiltration by polymorphs and some lymphocytes. There was well-marked fibrosis between the lung alveoli, and infiltration with mononuclears and some polymorphs was prominent. There were many alveolar phagocytes, and some giant cells were also to be seen. Blood vessels were largely normal, but a few could be seen, more especially near the small abscesses, in which the muscle coat showed some fibrinoid degeneration with endothelial proliferation. In these there was infiltration of the wall of the vessel by mononuclear inflammatory cells. There was no evidence of tubercle or sarcoidosis. The *lymphatic glands* showed chronic inflammatory changes only. The *pancreas* and *suprarenals* were normal. The *heart* muscle showed no abnormality, but there were one or two small vessels in the fatty tissue immediately next to the muscle which showed changes from the normal. These consisted of mononuclear infiltration in the wall, of endothelial proliferation, and very slight necrosis of the muscle coat. No abnormality in the vessels in the heart muscle itself was found. The *kidney* showed slight tubular epithelial desquamation and a little lymphocytic infiltration in the interstitial tissue. A few blood vessels showed a change similar to that seen in the sections of the lung and heart. (The appearances were very similar to those depicted in Fig. 15 in the paper of E. F. McKeown, 1947.) The *spleen* showed a reactive hyperplasia. The appearances in the *liver* were those of venous congestion. The *knee-joint* showed a typical rheumatoid change with cell proliferation, even to the formation of giant cells in a few places.

Case 2*

A female cotton-mill worker aged 48 was admitted to hospital on Dec. 15, 1946, complaining of cough, loss of weight, and arthritis. The onset of an acute polyarthritis characterized by pain, swelling, and stiffness of the knee-joints had occurred for the first time in April, 1946, previous to which she had been quite well. During the four weeks following the onset the wrists, elbows, and shoulders had been involved. In November, 1946, she started to complain of lassitude, palpitations, and dyspnoea, and since the onset of the illness she had lost 2 st. (12.7 kg.) in weight. She gave a previous medical history of recurrent attacks of bronchitis. There was no relevant family history.

On examination there was a morbilliform rash of the arms and trunk; the temperature was 100° F. (37.8° C.), and dullness and bronchial breathing were present at both lung bases. There was no evidence of abnormality in the heart, abdomen, or central nervous system. The blood pressure was 105/60. *Pathological investigations* at this time showed Hb 70% and white cells 8,900. *Radiological examination* of the chest revealed bilateral basal opacities indicative of consolidation and, above this, marked reticular shadows extending into the mid-zones. Pneumonia was diagnosed and a seven-day course of penicillin was given, in spite of which a pyrexia ranging between 99° and 100° F. (37.2° and 37.8° C.) persisted. Except for occasional rises of temperature to 103° F. (39.4° C.) the patient remained in this condition until Jan. 16, 1947. During this time repeated sputum cultures for tubercle bacilli were negative, the general bacteriological examination of the sputum revealed nothing abnormal, and the radiological appearances of the chest remained unchanged on repeated examinations. At the beginning of February, 1947, she developed a spiking temperature ranging between normal and 103° F. From this time her condition gradually deteriorated, and she became more anaemic. Blood examination showed: red cells, 2,570,000; Hb, 50%; serum albumin, 2.2 mg. per 100 ml.; serum globulin, 4.5 mg. per 100 ml.; serum sodium, 320 mg. per 100 ml.; chlorides, 533 mg. per 100 ml.; blood urea, 26 mg. per 100 ml.; W.R. negative. Agglutination tests: *S. paratyphi A* "H," *S. paratyphi B* "H," *S. typhi* "H," negative 1 in 20, Comp. *S. paratyphi B* "O," *S. typhi* "O," *Br. abortus* negative 1 in 20.

On March 24 oedema of the legs developed, and on the 27th the patient died.

*This case was kindly brought to our notice by Professor Robert Platt, of Manchester, who, having seen the observations of one of us (Ellman, 1947)—namely, the interpretation of the joint and pulmonary lesions as part of a "rheumatoid disease"—felt that the case, which was in the wards of the Manchester Royal Infirmary under the care of Dr. Fergus R. Ferguson, was of an analogous nature. We are much indebted to him and to Dr. Ferguson for kindly suggesting that we might include the case.

Post-mortem Examination (performed by Dr. J. T. A. Lloyd 36–48 hours after death).—The body was that of a slightly pale middle-aged woman. *Respiratory system*:—There were a few fine pleural adhesions on both sides, with some 50 ml. of straw-coloured fluid on each side. The lower lobes of each lung and the lower part of the upper lobe of the left lung were firm and hard to the touch. They were congested, and also showed small areas of consolidation together with minute abscesses containing a little pus. The appearances suggested a terminal bronchopneumonia with a fibrosing pneumonitis. The remainder of the lung tissue appeared normal. No evidence of tubercle or of sarcoid was seen in the lungs. The trachea was normal. The mediastinal glands draining the lungs were slightly enlarged, but showed no evidence of tubercle. *Cardiovascular system*:—The pericardium contained about 50 ml. of greenish-yellow clear fluid. The heart was slightly dilated but not enlarged. The myocardium was soft and somewhat pale. The mitral valve cusps were very slightly thickened along the free margins, but no evidence of any endocarditis was present in any valve. The blood vessels showed slight atheroma. The *intestinal tract*

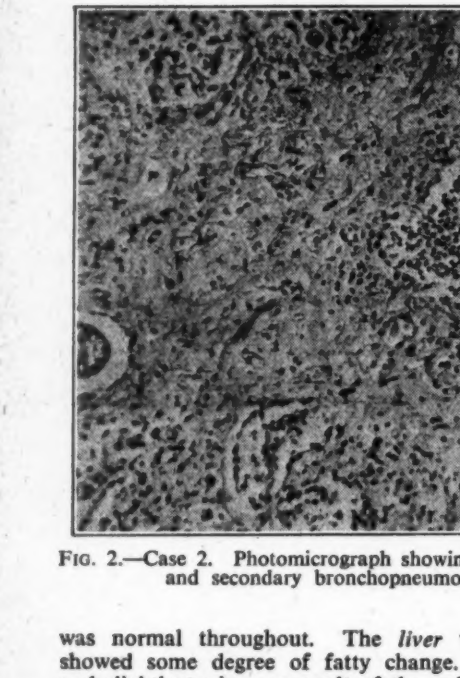

FIG. 2.—Case 2. Photomicrograph showing interstitial pneumonitis and secondary bronchopneumonia. (× 90.)

was normal throughout. The *liver* was not enlarged, but showed some degree of fatty change. The *spleen* was soft and slightly toxic as a result of the pulmonary infection. The *kidneys* showed no abnormality apart from some degree of pallor. There was a small cervical polypus, but the uterus and ovaries were normal. None of the organs revealed any evidence of tubercle or of sarcoidosis. The brain was not examined.

Histological Report.—Sections were cut from the kidney, spleen, lung, and lymphatic glands from blocks kindly supplied by Professor S. L. Baker. *Kidney*:—There were relatively few changes. Those present consisted of collapsed empty glomerular tufts, some tubular epithelial desquamation, and a few tubular casts. The blood vessels showed some atheroma only. The *spleen* revealed some reticular-cell proliferation with relatively empty sinuses. The *lung* (Fig. 2) showed considerable general disorganization. The main appearances were those of an interstitial pneumonitis with a terminal bronchopneumonia. The *alveoli* were of varying sizes, some being emphysematous, but many showed infiltration with polymorphs together with some mononuclear cells and also some desquamated alveolar phagocytes. A few of the alveoli were lined with cuboidal epithelium. However, the most striking change was seen in marked interalveolar fibrosis, with fairly well developed fibrous tissue which was infiltrated with mononuclear cells, plasma cells, and a few polymorphs. The blood vessels showed no change from the normal except that in one large vessel there was a little atheroma. There was no evidence of tubercle or sarcoidosis. The mediastinal lymphatic glands showed some chronic inflammation only.

Case 3

A housewife aged 55 was admitted into the rheumatism unit under the care of P. E. on Sept. 26, 1946, when she complained of pain, swelling and stiffness of the hands, shoulders, knees, and feet of three months' duration. There was no history of a precipitating factor in the form of an acute infection. Frequent attacks of tonsillitis had occurred during the past few years.

On examination she was thin and wasted; weight, 6 st. 9 lb. (42.2 kg.). No clinical abnormality was present in the heart, lungs, abdomen, or central nervous system. Examination of the locomotor system showed fusiform interphalangeal joint swellings and a swollen flexed left knee-joint. There was no lymphadenopathy.

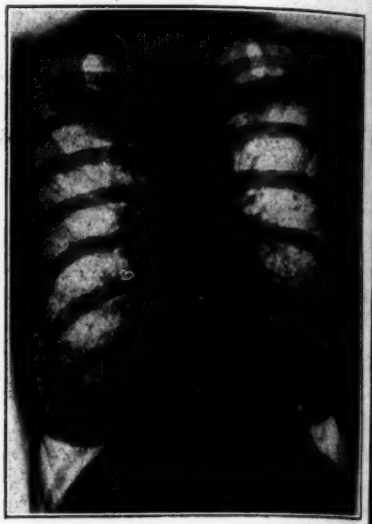

FIG. 3.—Case 3; Oct. 1, 1946. Radiograph of chest showing no gross abnormality.

Radiological examination of the chest showed no gross abnormality (Fig. 3). There were some calcified hilar foci; those of the hands and wrists showed osteoporosis and narrowing of the joint spaces.

Pathological investigations showed: E.S.R., 60 mm. in the first hour (Westergren); red cells, 5,920,000 per c.mm.; Hb, 102%; C.I., 0.85; white cells, 22,200 per c.mm. (polymorphs, 68%; lymphocytes, 26%; monocytes, 6%; eosinophils, 2%). Gastric residue before histamine: free HCl, nil; total acidity, 18 ml. N/10. Gastric residue after histamine: free HCl, 22 ml. N/10; total acidity, 44 ml. N/10. Urinalysis, N.A.D. Throat swab: no Klebs-Loeffler bacilli or haemolytic streptococci grown on Oct. 4, 1946; copious growth of haemolytic streptococci on Nov. 27; scanty growth of haemolytic streptococci on Dec. 5; W.R. and Kahn, negative; serum uric acid, 2.6 mg. per 100 ml.; alkaline phosphatase, 7.5 units.

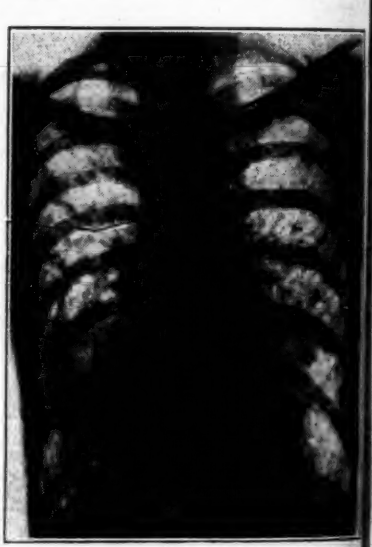

FIG. 4.—Case 3; June 16, 1947. Radiograph showing widespread heavy reticulation and miliary mottling throughout both lung fields.

The patient's general condition remained the same until June 12, 1947, when she complained of cough with sputum, sweating, and loss of weight of 7 lb. (44.5 kg.). There were now scattered rales throughout both lung fields, and the breath sounds were bronchovesicular in type. Serial skiagrams were unchanged until the one on June 16, which showed widespread heavy reticulation and apparent miliary mottling throughout the whole of both lung fields (Fig. 4). A presumptive diagnosis of pulmonary tuberculosis, Boeck's sarcoidosis or polyarteritis nodosa was made. Repeated sputum examinations and Loewenstein's culture, together with gastric lavage and concentration techniques, failed to

reveal the presence of tubercle bacilli. General bacteriological examination of the sputum revealed no abnormality. On Aug. 30 there was no significant change, and the radiological appearance of the lungs was regarded by several experts as being compatible with that of polyarteritis nodosa. A further radiograph on Jan. 16, 1948, showed the lung fields to be cleared a little, but heavy reticulation was still present. The patient now weighs 6 st. 2 lb. (40 kg.), but her general condition is fundamentally unchanged.

Discussion

In a recent discussion on the aetiology of chronic rheumatism one of us (Ellman, 1947) suggested that the theory of bacterial allergy or that due to foreign protein or hormones provided an attractive and rational aetiological basis for this rheumatoid state and at the same time strengthened the unitary theory. Fundamentally the acute and chronic rheumatisms may be regarded as anaphylactic diseases with multiple lesions in the mesodermal system produced by continual antigen–antibody reactions in or on tissue cells. Visceral and other lesions may be explained as hypersensitivity manifestations in tissues elsewhere in the body. Some co-ordination is thereby provided for the rheumatoid group of diseases and suggests a relationship between the acute rheumatoid type of arthritis and rheumatic fever.

It is possible, too, as has been suggested by Parkes Weber (1946), that the syndromes of a recurrent and transitory nature included under the term "palindromic rheumatism" of Hench and Rosenberg (1944) can be extended to include the so-called intermittent hydrarthrosis, serum joint disease, allergic arthritis, and allied syndromes. Again, the work of Rich and Gregory (1943, 1946) and their co-workers has indicated an even wider association on the basis of hypersensitivity between the rheumatoid type of arthritis and such hitherto obscure conditions as sclerodermia, dermatomyositis, polyarteritis nodosa, and acute disseminated lupus erythematosus. Bohrod (1947) has described their essential lesions as "rheumatoid granulomata," and Cecil (1946) refers to "these rheumatoid diseases of the collagen matrix." In clinical practice we have been impressed on more than one occasion by the association of sclerodermia with a rheumatoid type of arthritis (Ellman and Parkes Weber, 1948). While the experimental production in rheumatic fever of anaphylactic pulmonary lesions with a peculiar type of "pneumonitis" has received some attention (Rich and Gregory, 1943, 1946), pulmonary and other lesions are now known to occur also in such widespread systemic diseases as polyarteritis nodosa (Daley and Miller, 1946) and disseminated lupus (Rakov and Taylor, 1942; Klemperer, 1948).

So far as the lung lesions are concerned, Gouley (1938) and Neubuerger *et al.* (1944) found histologically in "rheumatic pneumonia" three successive stages of change in the interalveolar septa: (1) fibrinoid necrosis in collagen, (2) infiltration with round cells, plasma, and giant cells; (3) fibroblastic proliferation and fibrosis. All these are essentially changes in the collagen matrix.

In support of the anaphylactic or hypersensitivity theory in the mechanism of production of these lesions Rich and Gregory were able to carry out necropsy studies on patients with serum sickness. They found changes in the endocardium, myocardium, and pericardium, all of which were histologically indistinguishable from those in rheumatic fever. Further experiments have been carried out on animals rendered anaphylactic with horse serum or egg albumen. Similar changes were again produced in the heart, and more recently pulmonary lesions characterized by interstitial fibrinoid necrosis.

From those observations, and in view of the widespread systemic nature of some of the cases, it will be understood how the term "rheumatoid arthritis" is really misleading. "Rheumatoid disease" may be open to criticism, but it is preferable as the parent term, with joint lesions seen as the principal clinical manifestation, in the same way that the term "gout" describes the parent lesions of a metabolic dysfunction whose principal clinical manifestation is the joint involvement.

The three cases we have described exhibit common features in what appears to have been the development of lung lesions during the early active phase of the joint process. In Case 3 the onset of the lung disease is known from the serial radiographs to have occurred nine months after the onset of the polyarthritis, and attention was drawn to it by the symptomatology of cough, dyspnoea, and weight loss initially ascribed to possible pulmonary tuberculosis. All investigations disproved this diagnosis, likewise the possibility of Boeck's sarcoidosis. A consensus of expert opinion on the radiological appearances of the lung reticulation has favoured the diagnosis of polyarteritis nodosa, and the relationship of this condition with the "rheumatoid granulomata" is of considerable interest. It would be fair to postulate a hypersensitivity phenomenon involving equally the joint and lung tissues. In Case 2 symptoms referable to the pulmonary disease occurred six months after the onset of the polyarthritis. The radiological lung changes were those of a basal reticulation. Unfortunately no radiograph of the chest before this time is available.

In all three cases the clinical course is similar, the joint lesions preceding the pulmonary lesions, and one might not unreasonably assume, without wishing to appear to be in any way dogmatic, that the joint and lung lesions are manifestations of one and the same pathological process.

Studies of the two cases that came to necropsy present certain features in common, also suggestive on histological investigation and predominantly evident in the lungs, where fibroblastic thickening of the alveolar walls (chronic fibrosing pneumonitis), plus infiltration by mononuclear, plasma, and occasional polymorph cells, was present; the kidney in Case 1 revealed fibrinoid necrosis in a few blood vessels. This case also showed similar changes in blood vessels at another site—namely, in the fatty tissue immediately next to the heart muscle. In both cases the section of the lung has shown a chronic fibrosing type of "pneumonitis." It was certainly not sarcoid, and at the same time was rather different from the "rheumatic pneumonia" of acute rheumatic fever. Our own opinion was that the lung changes could not be dissociated from Gouley's Stage 3, already described, where interalveolar fibroblastic proliferation predominated on histological examination. However, it cannot be held that this histological change is specific by itself, but its being coupled with the necrosis found in the muscular wall of the artery in other parts of the body suggests that an acute arteritis had been present in the past as part of a fibrinoid necrosis. These arterial changes were found only after careful and thorough search, and, taken together with the lung lesions, would appear to suggest a widespread disseminated lesion. Further than that we are not prepared to go from the pathological studies alone. However, on clinical grounds the similarity of the lung lesions is undoubted, and many features of one are mirrored in the other.

It is of interest to note that Klemperer has recently reported a case of disseminated lupus erythematosus with lung lesions where the histology was of a fibrinoid necrosis in the interalveolar septa. A similar pathological process has been observed in the allied group of so-called granulomata already noted.

Summary

The widespread systemic nature of certain cases of rheumatoid arthritis has been noted.

It is suggested that "rheumatoid disease" is a preferable term whose principal clinical manifestation is "arthritis."

Three cases of joint and lung lesions are recorded, and it is suggested that they are among the clinical manifestations of "rheumatoid disease."

We are greatly indebted to Dr. J. N. Cumings for help on the pathological side, for the photomicrographs, and for his close study of the histology of Cases 1 and 2; to Dr. A. Signy for much helpful criticism; to Professor Robert Platt for kindly allowing us to include Case 2; and to Dr. G. Batten for help on the radiological side.

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CORD COMPLICATIONS DURING PREGNANCY AND LABOUR

BY

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Considering the length and slenderness of the umbilical cord, it is surprising that cord complications do not occur more frequently. Prolapsed cord, which is the commonest of these complications, occurred in only 50 cases out of a total of 10,000 deliveries—i.e., 0.5%. Munro Kerr (1937) gives an incidence of 0.25% and DeLee (1943) an incidence of 0.8%.

The 42 cases treated in this hospital are listed in Table I. Eight patients were admitted with dead babies and therefore received no special treatment A summary of the 50 cases is given in Table II.

Three of these cases are given in further detail because of their special interest.

Mrs. A., aged 35; 2-gravida; married 12 years. Admitted with severe pre-eclamptic toxaemia, not improved by rest. Surgical induction performed at 28 weeks with a Drew-Smythe catheter. At half dilatation, hand and cord prolapsed beside head. Attempt at reposition unsuccessful. Forceps then applied to foetal head, but, though small, the head was too large to be delivered through the thick half-dilated cervix. Two incisions made in cervix, and infant, weighing 2 lb. 8 oz. (1.13 kg.) delivered alive. Cervix sutured. Mother made uneventful recovery. Infant lusty at birth and remained healthy. It is now 2 years old.

This delivery may appear to be rather heroic treatment but is justified by results.

Mrs. B., aged 28; 2-gravida; admitted at term as a transverse lie. External version to vertex performed, and patient sent to *x*-ray department for pelvimetry. Membranes ruptured and cord prolapsed while patient was on the *x*-ray table. Patient was returned to the ward in the knee–chest position and the cord replaced through a quarter-dilated cervix. Pulsation in the cord returned after reposition, and caesarean section was performed. At operation the cord was found to be stretched tightly across the head, and the child was stillborn.

Mrs. C., aged 26; primigravida; term. Breech presentation at term. Fairly easy external version to vertex, but foetal heart became irregular and slow. A few minutes afterwards the heart returned to normal and the foetus was left as a vertex, with the head above the brim. Membranes ruptured early in labour, and the foetal heart became irregular. The head was still high, but when it was pushed down into the pelvis with a hand above the symphysis the foetal heart stopped altogether, returning as soon as the pressure was released. It was decided that this was the so-called "occult type" of prolapsed cord—i.e., the cord was probably nipped between the foetal head and the pelvic brim. Caesarean section was therefore performed and a healthy infant obtained. The cord was twisted loosely round the child's body, but the actual prolapsed loop was not seen, as it would be dislodged as the head was delivered.

Apart from prolapse of the cord, the following cord complications can occur:

Cord Round Neck or Body

With an active foetus, or with repeated antenatal versions, the umbilical cord may be wound round the neck or body once, twice, or three times. Only once have I seen the cord four times round the neck of the foetus. Strangulation *in utero* or during birth may result. This condition of the cord is usually recognized only during labour or at delivery, but in a few cases it can be diagnosed during pregnancy. The following three cases illustrate the point.

Mrs. D., aged 35; primigravida; breech presentation at term. Easy antenatal version, but directly after version the foetal heart dropped to 80. The heart rate gradually returned after a few minutes and the foetus was left in the vertex position. Labour started spontaneously a few days later. Delivery was normal, after a rapid labour, but the infant was stillborn, with the cord tightly round the neck twice.

Mrs. E., aged 35; primigravida. Breech presentation at 36 weeks. Easy antenatal version, but foetal heart stopped. Foetus was turned back to a breech, and the heart restarted as soon as the foetus reached the transverse position. This manœuvre was repeated the following week with exactly the same result. It was therefore concluded that the foetus had a short cord or the cord was round the neck, and that this would cause delay in delivery and probably stillbirth. It was decided to deliver by caesarean section at term. At operation it was found that the cord was twice round the infant's neck and that there was an area of haemorrhage at the root of the cord where it had been pulled upon during the antenatal version. The infant was healthy, weighing 6 lb. 15 oz. (3.15 kg.), and the mother made an uninterrupted recovery.

Mrs. F., aged 34; primigravida; term. Breech presentation. Easy version, but foetal heart dropped to 100 and became muffled and irregular. The foetus was turned back to a breech. A second attempt a few minutes later produced the same result, so that the foetus was left as a breech. In this case also caesarean section was performed at term, and the cord was found to be wrapped round the neck and body. The infant was healthy, and the mother made a satisfactory recovery.

Over-activity of the foetus with self-strangulation is illustrated by the next case.

Mrs. G., aged 29; 2-gravida. At 38 weeks the head was high and the foetal heart was heard. The patient was healthy, with a blood pressure of 120/68, no albuminuria, and a negative Wassermann. Three days before term the foetus became increasingly active and then all movements suddenly stopped. Labour began spontaneously, and when the membranes ruptured the liquor was deeply stained with meconium. The infant was stillborn and macerated, and the cord was wound tightly round the neck three times, with tension at the umbilicus.

Cord round the neck, apart from causing foetal distress, may prevent engagement of the head and so increase the duration of labour.

TABLE I.—*Summary of Cases*

Gravid	Maturity (Weeks)	Presentation	Dilatation	Method of Delivery	Infant
2	28	Head, hand, and cord	Half	Dilatation of cervix; forceps delivery	2½ lb. (1·13 kg.). Healthy, lived
1	28	Vertex	2 fingers	Internal version after reposition of cord; foot pulled down; normal delivery	3 lb. 9½ oz. (1·63 kg.). S.B.
1	38 (twins)	Breech (1st twin)	Full	Normal delivery	4 lb. (1·8 kg.). S.B.
3	28	Transverse	,,	Internal version to breech; normal delivery	2½ lb. (1·13 kg.). S.B.
2	28	Vertex; acute hydramnios	,,	Normal	2 lb. (0·9 kg.). S.B.
1	34	Vertex	,,	,,	4 lb. 4 oz (1·9 kg.). Healthy
4	36	,,	,,	,,	4 lb. 13 oz. (2·18 kg.). Healthy
	S.I. with Drew-Smythe catheter for toxaemia				
1	31	,,	,,	,,	3 lb. 15 oz. (1·78 kg.). Alive, but died during 1st week
	Acute pyelitis				
1	36	,,	1 finger	Caesarean	4 lb. 10 oz. (2·1 kg.). Healthy
	Induction with D.S.C. for toxaemia				
	Term	Transverse	Three-quarters	Internal version to breech; manual delivery	7 lb. 6 oz. (3·35 kg.). Healthy
2	40	Vertex	Half	Dilatation of cervix and forceps delivery	7 lb. 1 oz. (3·2 kg.). Healthy
1	,,	,,	Three-quarters	Forceps	7 lb. 10 oz. (3·46 kg.). S.B.
2	40	,,	Prolapse during surgical induction	Internal version to breech; normal delivery; caesarean not contemplated because of patient's general condition	9 lb. 9 oz. (4·34 kg.). S.B.
3	40	,,	Full	Forceps	6 lb. 12 oz. (3·06 kg.). Healthy
2	40	,,	,,	,,	6 lb. 2 oz. (2·78 kg.). Healthy
1	40	Breech	One-quarter	Caesarean	7 lb. (3·17 kg.). Healthy
1	40	Vertex	Full	Forceps	6 lb. 9 oz. (2·98 kg.). Healthy
2	40	Breech	One-quarter	Caesarean	7 lb. 7 oz. (3·37 kg.). Healthy
2	40	Vertex	Full	Forceps	7 lb. 8 oz. (3·402 kg.). Healthy
1	40	,,	,,	,,	5 lb. 10 oz. (2·55 kg.). Healthy
1	40	,,	One-quarter	Caesarean	7 lb. 5 oz. (3·32 kg.). Healthy
4	36	,,			
	S.I. for toxaemia				
2	40	Transverse	Full	Internal version to vertex; forceps	7 lb. 3 oz. (3·26 kg.). Healthy
5	40	,,	Three-quarters	Internal version to breech; manual delivery	11 lb. 3 oz. (5·07 kg.). S.B.
2	36	,,	,,	,, ,, ,,	7 lb. (3·17 kg.). S.B.
2	40	Vertex	,,	Forceps	6 lb. 12 oz. (3·06 kg.)
2	40	,,	One-quarter	Caesarean	S.B.
1	34 (twins)	Breech (1st twin)	Full	Manual delivery with forceps to after-coming head	5 lb. 11 oz. (2·58 kg.). Healthy
1	40	Vertex	Onset of labour	Caesarean	Healthy
1	40	,,	Half	Forceps on full dilatation	6 lb. (2·72 kg.). S.B.
2	40	,,	Full	Forceps	6 lb. 4 oz. (2·83 kg.). Healthy
2	40	Transverse	Onset of labour	Caesarean	7 lb. (3·17 kg.). S.B.
2	40 (twins)	,, (2nd twin)	Full	Internal version to vertex; forceps	7 lb. (3·17 kg.). Healthy.
5	40	,,	Half	Manual dilatation of cervix; internal version to breech; manual delivery	8 lb. 4 oz. (3·74 kg.). Healthy
1	40 (twins)	Breech (2nd twin)	Full	Manual	5 lb. 8 oz. (2·5 kg.). Healthy
1	40	Vertex	,,	Forceps	7 lb. 9 oz. (3·43 kg.). Healthy
5	40	,,	,,	,,	7 lb. (3·17 kg.). S.B.
2	36	,,	One-third	Manual dilatation of cervix and forceps	4 lb. 12 oz. (2·15 kg.). Alive. Died of cerebral haemorrhage
	S.I. for toxaemia and Rh-neg. blood				
2	40	,,	Three-quarters	Manual dilatation of cervix; forceps	7 lb. 8 oz. (3·4 kg.). Healthy
2	38 (twins)	Hand, foot, and cord (2nd twin)	Full	Internal version to breech; manual delivery	6 lb. 11 oz. (3·03 kg.). Healthy
2	36 (twins)	Transverse	,,	Internal version to breech; manual	3 lb. (1·36 kg.). Alive. Died of cerebral haemorrhage
	S.I. for toxaemia				
2	37 (twins)	Vertex	,,	Normal	4 lb. 4 oz. (1·9 kg.). Alive. Died of cerebral haemorrhage
	S.I. for toxaemia				
3	36	,,	During induction of labour	Caesarean	6 lb. 8 oz. (2·95 kg.). Healthy
	S.I. for toxaemia				

TABLE II.—*Prolapsed Cord*

Method of Delivery	Alive	Stillbirth	Neonatal Death	Total
Natural forces	4	9 (8 dead on admission)	1	13
Forceps	13	5	1	18
Caesarean	6	2	—	8
Internal version and manual delivery	5	6	1	11
	28	22	3	50

Living : 56%. S.B. : 44%. N.N.D. : 3%. Foetal salvage : 50%.

Mrs. H., aged 24, primigravida, had a labour lasting 48 hours. There was delay in descent of the head, and foetal distress developed early in the second stage. Forceps were applied and a healthy infant delivered weighing 6 lb. 11 oz. (3.03 kg.). The cord was short and was round the neck, preventing descent of the head and causing foetal distress.

Mrs. I., aged 38; primigravida; term. Head high throughout pregnancy and during labour. Pains fairly strong after rupture of membranes, but no descent of the head. Foetal distress appeared and caesarean section was performed. At operation the cord was found to be wrapped four times round the neck, preventing descent of the head and causing foetal distress. The infant was shocked at birth, but recovered. The mother made an uninterrupted recovery.

Foetal distress was the only sign in the following three cases:

Mrs. J., aged 32; primigravida; 36 weeks. Foetal distress at full dilatation. Foetal heart rate 80, with passage of thick meconium. Forceps delivery performed. No disproportion, but cord round the neck and both arms, and pulsating feebly. Pulsation restarted strongly when cord was unwound. The infant was healthy and weighed 4 lb. 7 oz. (2 kg.).

Miss K., aged 23; primigravida. Severe pre-eclamptic toxaemia at 36 weeks, with spontaneous onset of labour. Labour progressed normally until the end of the second stage, when the foetal heart suddenly stopped. The infant was stillborn, with the cord very tightly round the neck.

Mrs. L., aged 34; primigravida. Labour started spontaneously, but foetal distress occurred at the beginning of the second stage. Forceps were applied, and a healthy infant weighing 5 lb. 15 oz. (2.7 kg.) was delivered. There was no disproportion, but the cord was wound tightly round the neck, causing foetal distress.

These last few cases show the importance of frequent auscultation of the foetal heart throughout the second stage of labour and the need to have everything ready for a rapid forceps delivery in such an emergency.

A short cord may cause delay in descent of the head and foetal distress, but I have not had a case of this sort requiring operative intervention in my series.

True Knot in the Cord.—A true knot in the cord is often seen after delivery, but in most cases it is formed during delivery, when a loop of cord is slipped over the infant's head or shoulders. True knots can occur *in utero*, especially after antenatal version or with a very active foetus. I have myself seen only one case of a true knot which might have been the cause of stillbirth, but this occurred in a patient with severe pre-eclamptic toxaemia. There was a tight knot in the macerated cord, but death

might have been due to maternal toxaemia. A case of true knot in the cord causing foetal distress during labour was described recently by Price (1947).

Incidence of Cord Complications

Cord complications are rare, but the foetal death rate due to them is very high. DeLee gives the foetal death rate in treated cases as 40–50% and in untreated cases as 80%. In this series the foetal death rate in treated cases was 40.5%. Because of this rarity it is difficult for any one person to get sufficient experience in the treatment of cord complications, and this is one reason why the foetal death rate will always remain high. Early diagnosis and adequate treatment are essential, and two necessities for treatment are an intelligent and well-trained nursing staff and a resident obstetrician.

Diagnosis and Treatment

The diagnosis of prolapsed cord may be made first by seeing the cord presenting at the vulva. More commonly the first indication is slowing of the foetal heart, the cord being found on routine vaginal examination. In a few cases the cord is nipped at the pelvic brim and cannot be felt with the examining finger.

The treatment of prolapsed cord depends on the presence or absence of foetal heart sounds and on the degree of dilatation of the cervix. In all cases except where the cord is macerated the patient is placed in the knee–chest or the high Trendelenburg position while preparations for further treatment are being made. Pressure on the cord can further be relieved by the operator inserting two fingers into the vagina and holding up the presenting part above the brim. Even when pulsation has ceased, relief of pressure on the cord sometimes restores the circulation, but the foetus cannot stand total obstruction of the cord for more than a very few minutes. The knee–chest or Trendelenburg position, though useful in an emergency, can be maintained for only about 10 to 15 minutes without great discomfort to the mother. When operative intervention is to be used the patient can be anaesthetized in the Trendelenburg position, and should be moved only when the operator is ready to begin. If the cervix is as much as three-quarters dilated, then immediate delivery is performed —by forceps in a vertex presentation or by manual delivery of a breech or transverse lie. In such circumstances there is no need to waste time trying to replace the cord. When the cervix is less than three-quarters dilated the difficulties are increased.

Reposition of the cord can be attempted, but this, easy in theory, is very difficult in practice, and the actual reposition may cause further foetal distress by pressure and kinking. If this method is tried the hand is the best repositor, but the cord is an awkward and slippery organ with a will of its own. The foetal heart must be counted at least every five minutes after reposition in case of further pressure as labour progresses. In one case it seemed to me to be a good idea to give an injection of nikethamide into the cord before reposition, and this was tried. The foetal heart improved in tone and frequency, but the cord continued to bleed at the site of injection.

Internal version to a breech presentation is not satisfactory. The idea is that the breech fits less closely into the brim and so leaves more room for the prolapsed cord. In practice this does not work very well, because the cord may become entangled round one leg or the child may sit down on it at the level of the brim.

Caesarean section is the method of choice when the cord is pulsating strongly, the cervix is less than three-quarters dilated, the operating theatre is available, and the operation is quick. It is no good subjecting a mother to caesarean section for prolapsed cord if the infant is going to be stillborn. She can have her stillborn infant without the added discomfort of an abdominal incision.

There were no maternal deaths in this series. Though the foetal results are poor, they can be improved by constant watchfulness on the part of the midwife and by quick and accurate diagnosis by the obstetrician, with minimum delay in treatment.

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HODGKIN'S DISEASE CONFINED TO THE JEJUNUM

BY

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Pathologist to the Seamen's Hospital Society

The subvariety of Hodgkin's disease affecting the alimentary tract, though by no means excessively rare, is better described in journals than in textbooks. A clear outline of its features, with references to date, is given by Hayden and Apfelbach (1927), who selected 26 previously reported cases for their study, adding three of their own: spleen and liver are not enlarged and nodules within them are uncommon; mesenteric but not other groups of lymph nodes are involved; lesions in the gut tend to be multiple and small, starting in the mucosa or submucosa, forming an ulcer with an enclosing "wall," and quickly penetrating muscular and serous coats; histologically, lymphocytes and endothelial cells predominate, while Sternberg–Reed cells are scanty; symptoms are intestinal and not of long duration; death often follows perforation or haemorrhage, or is cachectic.

The case here presented conforms to the above description and is very similar to that published (without necropsy) by Badia (1943) of a woman aged 29, with a six-months history, who died seven weeks after a loop of small intestine had been resected and diagnosed histologically as Hodgkin's sarcoma of the jejunum.

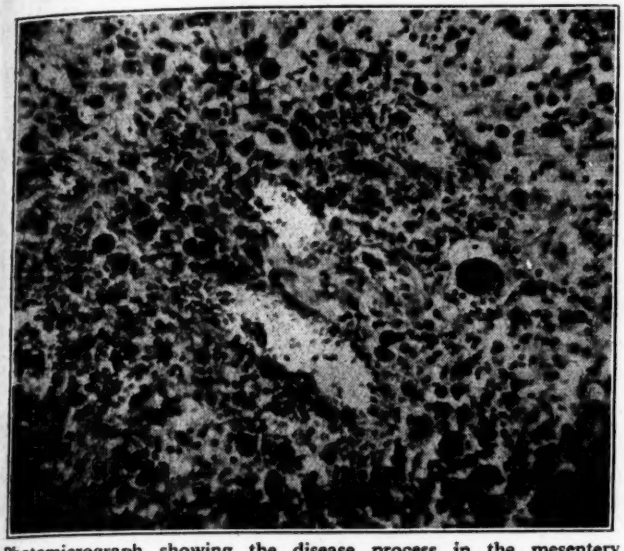
Case Report

A ship's chief wireless operator, aged 51, was admitted to the Dreadnought Seamen's Hospital on June 20, 1947, with a three-months history of burning epigastric pain two hours after meals, loss of 1 st. 7 lb. (9.5 kg.) in weight, loss of appetite, and weakness of the legs when climbing ships' ladders. Vomiting had not occurred and the bowels were regular. Except for pneumonia eleven months before (Long Island College Hospital), his health had been good. His mother had died at 84 (heart) and father at 79 (cancer of stomach); two brothers and a sister were alive and well. Physical examination revealed wasting, very bad teeth, and no palpable glands. Weight was 6 st. 12 lb. (43.5 kg.), blood pressure 110/70 mm. Hg., pulse 100 (and higher thereafter), temperature 96.2° F. (35.7° C.), but between 99 and 102° F. (37.2 and 38.9° C.) thereafter.

The following investigations were carried out. Radiograph of chest: chronic bronchitic changes. Barium meal: stomach and duodenum appear normal. Barium enema: there is a filling defect in the sigmoid. Urine: no chemical or microscopical abnormality. Wassermann and Kahn: negative. Alcohol-histamine meal: no abnormality. Blood count: haemoglobin 53% (Haden); R.B.C. 3.2 millions and W.B.C. 6,200 per c.mm.; colour index 0.83. Sedimentation rate (Westergren): 24 mm. at one, 49 mm. at two hours. Blood urea: 30 mg. per 100 ml. Plasma protein: 5.25% (albumin 3%/globulin 2.25%

= 1.3). Occult blood: strongly positive benzidine test, negative amidopyrine test. Sputum: four times negative for tubercle.

Carcinoma of the colon was diagnosed, and laparotomy was performed (July 8) after transfusion had raised the haemoglobin level from 47 to 61% (Haden). An adhesion between sigmoid and small intestine was freed and the resulting hole in the colon closed. An abscess cavity was found in the mesentery, to which small intestine was bound. The loop and mesentery



Photomicrograph showing the disease process in the mesentery adjacent to the surgically excised loop of jejunum (× 190).

were resected, and from them a histological diagnosis of Hodgkin's disease was made (see Fig.). The patient died on the fifteenth post-operative day.

The specimen removed at operation consisted of a piece of jejunum 24 cm. long with attached mesentery up to 5.6 cm. wide, incised about midway, where the gut was thickened, haemorrhagic, and bunched by fibrosis, to show a brawny bile-stained excavation, defined by scar tissue, extending 3 cm. from the incised gut into the mesentery. A ragged gaping hole, occupying most of the free aspect of the thickened jejunum opposite this excavation, was caused by surgical dissection. There was thus evidence of a swollen, fibrosing, penetrative lesion encircling the middle 5 cm. of the loop of gut resected and rather abruptly demarcated from the remaining gut, which was of normal appearance. The lymph nodes in the attached mesentery were enlarged up to 1.3 by 0.8 by 0.7 cm. and showed uniform yellow glistening cut surfaces.

The necropsy showed general purulent peritonitis, with a number of tough fibrous adhesions in addition to the fibrin binding loops of the small gut. These adhesions were found to occur on the serosal aspect of ulcers in the upper jejunum, where roughening, slight puckering, and fibrous tags but no tubercles were seen. There was no gross abnormality of stomach or duodenum. The uppermost lesion was a shallow ulcer, 1 by 0.6 cm., situated a few centimetres beyond the duodeno-jejunal flexure, with its axis transverse to that of the gut, with its floor short of the muscularis, and with its edges sheer. This was the only ulcer without accompanying fibrous adhesions on the serosa. The next lesion, 80 cm. below the flexure, was the anastomosis representing the site of the surgically excised loop, with considerable sepsis in the adjacent mesentery. Below this, at a point 140 cm. (pre-operatively 164 cm.) from the flexure, came a group of four small ulcers (largest 0.8 cm. diameter) of punched-out appearance, with sloughing floors piercing the muscularis. An area, about 2.5 cm. in diameter, of faint white stippling could be seen infiltrating the mucosa throughout this ulcer-bearing zone when it was brightly illuminated; there were also a few slit-like erosions about 1 mm. long. Below this group, 170 (pre-operatively 194) cm. from the flexure, was a single girdle-type ulcer measuring 2 by 0.8 cm., with its floor penetrating the muscularis and with its edge raised, swollen, and mainly rounded, smooth, and tense-looking, though eroded in places. Another similar though slightly smaller ulcer occurred 200 (pre-operatively 224) cm. below the flexure. Next below this, 230 (pre-operatively 254) cm. from the flexure, came the largest of the lesions, which consisted of an ulcer, 6.2 by 2.2 cm., encircling the gut for about two-thirds of its circumference. In contrast with the other lesions the ulcer floor was in this case hypertrophied, so that it stood up as a plateau 0.3 cm. above the mucous membrane; it was coarsely nodular, fissured, and stained slate-colour by altered blood. A smooth, tubular, and slightly undermined edge, itself ulcerated in places, surrounded it like a rail. Two more adjacent punched-out ulcers (the larger measuring 1 cm. in its longer axis, transverse to the gut) were found beyond this at a distance of 240 (pre-operatively 264) cm. below the flexure, and here the lesions ceased. A short Meckel's diverticulum was present. The colon was distended by pale sprue-like faeces. Mesenteric lymph nodes were moderately enlarged up to 1.8 by 1.5 by 1.2 cm. and showed uniform yellow cut surfaces. There was no enlargement of other groups. The spleen was firm and below normal size.

Comment

The histology of Hodgkin's disease is present only in sections of the gut lesions, the affected piece of mesentery (where the picture is most typical), and the larger of the mesenteric lymph nodes. In most sites the changes appear to be early and rather atypical. In some nodes large Hodgkin-like cells are scattered diffusely and the cells of the sinuses are proliferating without destruction of normal architecture. Fibrosis in the nodes is only beginning, and typical giant cells have to be searched for. Sections of the ulcers show necrosis of the base with replacement of all coats by granulation tissue containing a variety of chronic inflammatory cells together with small hyperchromatic giant cells, and affected by pyogenic infection to varying degrees. In one cut, at the periphery of an ulcer, the muscularis mucosae is seen breaking up beneath a mucous membrane which is still intact. In all regions there is a prominence of cells of reticulo-endothelial type, as noted by Hayden and Apfelbach (1927) and also mentioned in the report of a case of gastric Hodgkin's disease by Jungmann (1943). These cells, tending to be diffusely scattered, to show distinctly eosinophil cytoplasm and rather well-defined outlines, sometimes look at first glance like the expected infiltration of eosinophil polymorphs, which is not a noticeable feature in these sections. Intravascular plugs of granulation tissue, sometimes mixed with thrombus, are common and often contain small hyperchromatic giant cells. It seems possible that this invasiveness for blood vessels may by infarction play a part in the production of the ulcers. Vascular penetration has been photomicrographed both by Donati and Bragaglia (1942) in an intestinal case and by Bini and Parvis (1940) in a gastric case. Histological malignancy is stressed in both these cases. In the present case the short history, the small hyperchromatic giant cells, and the cellular rather than fibrotic reaction are held to indicate simply an early and acute form of Hodgkin's disease.

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The Third Annual Report of the Liverpool Cancer Control Organization has some interesting figures relating to cases of cancer referred for treatment during 1944. Among 2,668 cases the disease was so advanced as to render treatment impracticable in 993. Of the 1,675 cases in which treatment could be undertaken there were only 971 in which the condition was at a sufficiently early stage to warrant radical curative treatment being attempted. Of the 971 cases so treated 72 subsequently died of intercurrent disease or were lost sight of. There remained for review 899 patients, of whom 617 were alive three years after the start of treatment.

Medical Memoranda

Traumatic Rupture of Bowel in Inguinal Hernial Sac

Factors predisposing to this injury are irreducibility of the hernia, distension of the bowel, and nipping of the bowel against the unyielding surface of the pubic bone. A truss may therefore be a source of danger if it does not completely control the hernia and if the patient sustains an injury which presses the truss and, in turn, the bowel back against the pubis.

The following case shows that rupture of the bowel may occur in these circumstances and may lead to a fatal result.

Case History

A man aged 76 had worn a truss over a right oblique inguinal hernia for 30 years. On April 4, 1947, he tripped and fell forward on his face. Immediately after the fall he felt a dull constant pain in the hernia, which had come down. He therefore reduced the hernia without difficulty, although a small lump remained. Severe epigastric pain soon began; at first this was made worse by movement and relieved by lying down, but within half an hour of the accident it appeared to assume a colicky nature, causing the patient to roll in agony. He vomited twice and went to bed. During the night the pain gradually subsided, but vomiting was repeated three or four times. The next day he experienced stabbing pains on movement, and when he coughed there was pain in the hernia. Vomiting continued and his doctor attempted, without success, to reduce the lump in the right inguinal region.

On admission to hospital 30 hours after his fall the patient complained of generalized abdominal pain, which was constant and was made worse by movement. His bowels had not functioned since the accident.

On examination he was very short of breath and had a constant cough with white mucous expectoration. The tongue was dry and furred; temperature 97.6° F. (36.4° C.), pulse 106, respirations 45. *Cardiovascular*: Blood pressure 135/85; no oedema, slight cyanosis, cardiac enlargement to left (apex beat 4¼ in. (11.25 cm.) from midline). *Lungs*: Normal percussion note; breath sounds vesicular; basal rales, scattered rhonchi, both inspiratory and expiratory. *Abdomen*: Did not move on respiration; slight distension, no visible peristalsis; generalized tenderness and rigidity, most pronounced on right side; marked hyperaesthesia in right iliac fossa. *Per rectum*: Tenderness in pouch of Douglas; no mass palpable. Over the external inguinal ring there lay a slightly tender lump, 1½ in. (3.75 cm.) in diameter. A diagnosis of peritonitis due to perforated gut was made.

Operation.—Laparotomy was undertaken under spinal "nupercaine" (Dr. Henry Williams). A right lower paramedian incision was made and the tissues at the lower end were stripped down so as to expose the inguinal lump. This consisted of bruised and oedematous sac and appeared to be empty. On incising the peritoneum a large quantity of thin purulent fluid escaped. Coils of small intestine were found lightly adherent and bathed in pus in the right iliac fossa. Generalized peritonitis was present. A perforation ½ in. (1.25 cm.) in diameter a few feet above the ileocaecal junction was closed with two layers of sutures. As the patient's condition at this stage was very poor the neck of the empty hernial sac was rapidly closed with cotton sutures applied from the abdominal aspect, and the abdomen was closed with drainage of pelvis and wound. On return to the ward he was in poor condition—blood pressure was 60, pulse 120, with frequent dropped beats.

On April 6 the blood pressure was 130/78, pulse 110, apex rate 120. Auricular fibrillation occurred and "digoxin," 0.5 mg. intravenously, was given, being repeated eight hours later. Next day the patient was irrational. Pulse was regular at 120. At 10.30 a.m. he suddenly became dyspnoeic and cyanosed, and died. Permission for necropsy was refused.

Comment

There is no direct proof that the ruptured loop of ileum occupied the hernial sac at the time of injury. On the other hand, the initial pain was felt in the hernia and abdominal symptoms did not supervene until after its reduction. These facts, together with the bruised condition of the sac as seen at operation, make it highly probable that rupture took place in the sac. It is suggested that the bowel was nipped between the head of the truss and the pubic bone.

I am indebted to Dr. J. Thomson, medical superintendent of Dunedin Hospital, and to Professor Gordon Bell for permission to publish these notes.

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Sternal Swelling as a Presenting Sign of Hodgkin's Disease

Goldman and Victor (1945), in reviewing the salient features of Hodgkin's disease, stress the importance of involvement of sternal nodes in that they accept it as a pathognomonic sign. All glandular areas may be enlarged in Hodgkin's disease, but involvement of sternal nodes might easily be overlooked, and it is my impression that the frequency of its occurrence is not appreciated enough. Experience has taught me to look for enlargement of the sternal nodes along the course of the internal mammary artery in each case suspected of this disease. If these glands are involved there may be a firm swelling at the level of the second and third intercostal spaces fixed to the underlying chest wall.

In treating several hundred cases of Hodgkin's disease with deep *x*-ray therapy I can say that roughly 15% of my patients at some stage showed an involvement of these lymph nodes, but in one case I found it to be a presenting sign. The following is the history of this case.

Case Report

On Nov. 20, 1946, a girl aged 15 attended the out-patient department of the Coventry and Warwickshire Hospital complaining of general weakness, slight loss of weight, unproductive cough, and a painless "swelling on the chest" which had appeared two weeks previously.

On examination a firm swelling lateral to the sternum was found at the level of the second intercostal space. Clinical examination of chest, heart, etc., revealed nothing abnormal. Radiography of chest and ribs revealed an azygos lobe and normal pulmonary fields, no enlargement of hilar glands, and a destructive lesion in the anterior end of the second right rib. A blood count showed 12,800 white cells, otherwise there was no abnormality. The E.S.R. was 23 mm. in the first hour. The Wassermann reaction was negative.

The patient was admitted to hospital, and exploration of the swelling revealed "caseous yellowish tissue" and destruction of the medial end of the second right rib. Suspicion of a tuberculous lesion was raised. The histological report was as follows: "No evidence of tuberculosis, but the picture is obscured by very pyogenic inflammatory changes." Examination of her sputum showed no tubercle bacilli.

On Feb. 12, 1947, she developed pain in the right chest and the external swelling became larger without fluctuation. She was again admitted, and a further radiological examination revealed destruction of the anterior end of the second rib and of the sternum and also general loss of translucency of the right lung without mediastinal shift; the left lung was normal. Bacteriological investigations of the aspirated pleural fluid, which was greenish yellow, showed only scanty mononuclear cells, and the culture was sterile. There was a leucocytosis of 29,600 with 91% polymorphs. A diagnosis of acute osteomyelitis was considered. A biopsy of the rib was taken, and the pathologist reported: "Section shows very severe pyogenic inflammatory changes; there is no evidence of tuberculosis or of a neoplasm in the material submitted." There was no response to a course of penicillin treatment.

The patient was then referred to me for an opinion about the advisability of *x*-ray treatment. Reviewing the case with the pathologist, he reported further on the slide, as follows: "At first sight the histological appearances suggest a subacute pyogenic inflammatory lesion, with an unusual predominance of eosinophils, but closer inspection reveals large numbers of reticulum cells, often multinucleate, of Dorothy Reed type. The appearances are those of Hodgkin's disease partly obscured by gross superimposed pyogenic infection." At the end of March, 1947, an enlargement of a gland in the left axilla was noticed, and its biopsy section showed "all the classical features of Hodgkin's disease at an active and relatively early stage of development." Later, enlargement of other glandular areas of discrete nature developed, giving the characteristic appearances clinically.

This case illustrates the value of enlargement of sternal nodes in the diagnosis of Hodgkin's disease. The striking feature in this particular case is the early appearance of this sign; indeed it was the only abnormal physical sign at the time of the first examination.

I wish to thank Mr. H. Morton Anderson and Dr. W. C. MacC. Wilson for their co-operation in this case.

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Reviews

ENDOCRINOLOGY

Textbook of Endocrinology. By Hans Selye, M.D., Ph.D., D.Sc., F.R.S.(Canada). With a preface by Professor B. A. Houssay. (Pp. 914 ; illustrated. $10.24.) Montreal : Acta Endocrinologica, Université de Montréal.

In a tribute prefacing this important book Professor Houssay writes: "This book represents a critical and concise, orderly presentation of what is most important in the immense collection of facts of modern endocrinology, a science so vast that there are specialists in numerous branch problems and few who know this entire field of study"; and "the limitations of space [actually 868 pages] oblige him to be somewhat dogmatic in his exposition." Selye, in his introduction, writes that his book represents a miniature of an "encyclopaedia of endocrinology" that is being prepared for publication and for the basis of which some 250,000 articles and books have been collected.

The first chapter, on the steroids, is a fascinating physico-chemical introduction to the science of endocrinology made relatively intelligible to the uninitiated by symbolic figures and diagrams. The theme is an appropriate bridge into the next chapter on the adrenals with their multiple secretion of vital steroids by the cortex. The author discusses fully the glycogen corticoids (corticosterone group) and enumerates four tests for gluco-corticoid activity. His account of the pituitary adreno-corticotrophic hormone is perhaps inadequate in view of many interesting papers that were presented at the 1947 meeting at Atlantic City of the Association for the Study of Internal Secretions. Of acute Addison's disease he writes that "death may occur with epileptiform or angina-pectoris-like symptoms"—a rather uncharacteristic description, as might be said of what he calls the chronic nervous or solar type of chronic Addison's disease, in which "melancholia or spells of acute delirium with maniacal excitement occur." These statements are not untrue, but an urge for classification and sub-classification somewhat obscures the clinical background and phase upon which such features may be superimposed. In his account of the physiology of the posterior pituitary he might have said more about the important work of Verney and colleagues on the effect of water (or deprivation of it) and salt and of emotion on the secretion of the antidiuretic hormone. A very interesting section—on a topic often neglected—is the one on the effect of extirpating various endocrine glands on the structure of the hypophysis. The remark that Simmonds's disease is about four times more frequent in the female sex is an understatement and does not take into account Sheehan's fundamental work in Glasgow, to which, surprisingly, I could find no reference. The inclusion of Simmonds's disease together with pituitary dwarfism and Fröhlich's syndrome in omnibus descriptions of the symptomatology, etc., of anterior-lobe hypofunction has obvious disadvantages. The statement that "Cushing's disease may be difficult to differentiate from Cushing's syndrome" leaves the reader rather puzzled.

The account (including historical aspects) of the morphology, pharmacology, and physiology of the ovaries is refreshingly stimulating and clear. He mentions ovarian agenesis and its description both by Turner and by Albright. There is an imposing classification of ovarian tumours, and he describes some associated clinical pictures. He does not discuss the fundamental work of Scowen on the nature and treatment of metropathia haemorrhagica. The experimental and clinical chapters on the pancreas and parathyroids are well done and among the best in the book, but the chapter on hypothyroidism is not adequately illustrated. He briefly mentions the important influence of tracer studies with radioactive iodine on the physiology and pathology of thyroid function. The therapeutic use and limitations of radioactive iodine in carcinoma of the thyroid are indicated, but this physico-chemical approach to the cure of thyrotoxicosis does not appear to have caught my eye; nor is there reference to the valuable work of Rawson and colleagues in this field at the Massachusetts General Hospital. A striking and useful chapter on the general-adaptation syndrome ends this remarkable book. To point out certain minor inadequacies, or to say that the historical, experimental, and physiological sections are more satisfying than the clinical, is no detraction from a splendid achievement in the complex and rapidly changing field of endocrinology, for which we are fundamentally indebted to Selye.

S. LEONARD SIMPSON.

THE MENTALLY UNBALANCED

Le Déséquilibre Psychique. Ses psychoses—sa morale. By Dr. J. Borel. (Pp. 380. 360 francs.) Paris: Presses Universitaires de France. 1947.

The subject of this monograph, the "mentally unbalanced," is one of the wide clinical concepts for which French psychiatry has shown a preference since the last century. It comprises a large group of constitutional mental abnormalities ranging from the mild eccentricity sometimes seen in artists to severe forms of antisocial psychopathy, drug addiction, and alcoholism. Borel sees transitions everywhere and so many mixtures of symptoms that he does not even attempt to discriminate and form distinct groups. The book is mainly descriptive, and its strength is the lively and clear portrayal of people suffering from all types of personality deviation. He compares their differences with the individual variations among normal human beings and mainly blames heredity for their abnormal conduct.

In the first part he discusses the mentally unbalanced person, describing his mental make-up in terms of the common-sense psychology unfortunately so often used in clinical psychiatry which prevents the development of more precise and scientific discussion of the psychology of the abnormal. In the second part he draws attention to certain psychotic reactions characteristic of and modified by the unbalanced nature of the underlying personality. In the last part, on the patients' morale, he describes and discusses criminal propensities and especially sexual perversions due to lack of psychological balance. Final remarks on the legal responsibility of the mentally unbalanced are inspired by the same philosophical attitude of the wise and experienced clinician which distinguishes the work as a whole.

W. MAYER-GROSS.

DYING AND RESUSCITATION

Dying, Apparent Death and Resuscitation. By S. Jellinek, M.D. (Pp. 263. 10s. 6d.) London: Baillière, Tindall and Cox. 1947.

This book is written in a discursive style which is seldom found in modern scientific works. In parts this contributes towards interest and readability, but it tends also to obscure the fundamental points which are considered to be at issue. The author has obviously studied his subject deeply and read widely. One of the results is that we are given momentary glimpses of the death beds of Rabelais, Goethe, Verdi, Napoleon, Seneca, and others, and are reminded of the comments of Homer, Cicero, Tacitus, and our own Will Shakespeare. These are all very interesting, but one is left wondering whether the author is explaining these historical, and even legendary, references in terms of his own beliefs or whether he is advancing them as evidence of the validity of these beliefs. We are not likely to be increasingly alarmed by the knowledge that Chopin stipulated that in the event of his (apparent) death he should be subjected to "the heart incision" before being consigned to the tomb, and surely it is inaccurate to suggest, as the author does, that at the present time there are many doctors who make the same stipulation.

Professor Jellinek does well to remind us that we should ponder over the origin of the process of dying, as distinct from the commonly accepted causes of death. But it hardly seems necessary to make a mystery of why people with heart disease die suddenly while engaged in heavy work. It would seem that the "originator" is as apparent in such cases as in those of biophysical and biochemical origin which he instances. And again, why must it be accepted that a sudden collapse after an injection of eucaine (benzamine hydrochloride, dose unspecified) is of psychical origin or due to the pain of acupuncture? In discussing the "scope and potentialities of the psychicum in the dying process" the author tends to become metaphysical. When he says that in the death agony "the life-principle and the indwelling tension (potentiality) in each separate cell seek to maintain themselves," that may or may not be intelligible to physiologists. But what are we to make of the contention that "the very fact that it is movements of the emotions, which are

of ethical significance—the worlds of ethics and of energy are entirely foreign to one another—which fill up the content of consciousness and lend to the clinical emotional phenomenon (the intra-agonal interval) its peculiar stamp, will hardly permit of the assumption that the course and starting point of this emotional activity is to be sought in the physical sphere, i.e. in energetic processes of the nerve-cells." Professor Jellinek wishes to tell us, I think, that on earth, as in heaven, there are more things than are commonly dreamed of in our everyday medical philosophy.

The second part of the book is a review of present-day life-saving procedures and indications for their improvement, which the author considers is much needed. In particular he stresses the dangers which attend the elimination of intrathoracic negative pressure by unnatural compression of the chest, and, conversely, the beneficial effects on the circulation of methods which more successfully simulate the natural variations of pressure within the thorax. It is strange, therefore, to find no reference in the book to Eve's rocking method of artificial respiration, which appears to meet the requirements of the author more closely than any of the other methods described. Professor Jellinek concludes with a plea for a national centre for life-saving information and technique through which the subject might be taught more widely, more thoroughly, and with greater emphasis on the practical problems involved.

SYDNEY SMITH.

DEVELOPMENT OF SCIENCE

An Outline of the Development of Science. By Mansel Davies. The Thinker's Library, No. 120. (Pp. 214; illustrated. 3s. 6d.) London: Watts and Co. 1948.

The author of this agreeable little book is a physical chemist, but he has not yielded to the temptation to give much more space to the wonders of physical and chemical science than to the less spectacular history of the biological sciences. His book is admirably written, and could, I think, be read with pleasure by any intelligent person. The two or three pages devoted to modern bacteriology and immunology are a model of accurate summarization, although some may doubt whether, *as a bacteriologist,* Koch *was* second to Pasteur. Dr. Davies quotes Bertrand Russell's sneer that Newton "was honoured by monarchs; and in true English spirit, was rewarded for his work by a Government post in which it could not be continued." Even Governments deserve fair play: it seems quite certain that Newton ardently desired the post which he was given and *very* doubtful whether even a modern police State could have forced him to go on doing work which he, for psychological reasons, no longer wished to do.

MAJOR GREENWOOD.

In *A Handbook for Nursery Nurses,* by Mrs. A. B. Meering, S.R.N. (Baillière, Tindall and Cox; 17s. 6d.), there has been gathered for the first time into one book a reasonably complete account of all that a pupil nursery nurse needs to study. Mrs. Meering, writing from her wide experience of nursery work, approaches the subject of training in child care from the practical side and seldom forgets that she is writing for young girls the majority of whom will not have had a vestige of scientific training. In the earlier days of nursery work most of the emphasis was on the physical care of the child, and provided he was well fed, was kept clean and tidy, and put on weight it was thought that little more was needed. In recent years the pendulum has tended to swing in the opposite direction and the fascinating study of the growth of the child's mind and character has sometimes obscured the study of the care and protection of his very susceptible body. Mrs. Meering holds the balance fairly between these two points of view, and the student who is guided by her book will make a good start towards learning to watch and care for a child as a whole personality—growing in mind and body. Her chapters on mental growth, play, and child management would be helpful to mothers as well as to students and to not a few nurses and doctors. Some chapters—for example, those on anatomy—are perhaps more detailed than necessary, but they are useful for reference. On the other hand, the section on the cause of infection and its prevention might well be amplified. The subject is difficult to teach to the uninitiated, but it should be possible to make more use of the descriptions of nursery technique as a means of illustrating the methods of preventing infection, since practically the whole of nursery hygiene has its basis in the ubiquity and troublesome habits of pathogenic organisms. However, this is a sound book even though, as Prof. Moncrieff says in his foreword, one may disagree with the author on some points of detail.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

Fractures and Orthopaedic Surgery for Nurses and Masseuses. By A. Naylor, Ch.M., M.B., M.Sc., F.R.C.S., F.R.C.S.Ed. 2nd ed. (Pp. 296. 17s. 6d.) Edinburgh: E. and S. Livingstone. 1948.

This edition contains new material on the use of penicillin.

The Driving Forces of Human Nature. By T. V. Moore, Ph.D., M.D. (Pp. 461. $6.50.) New York: Grune and Stratton. 1948.

An introduction to the psychology of normal and abnormal emotional behaviour and volitional control.

Practical Bacteriology, Hematology, and Parasitology. By E. R. Stitt, M.D., Ph.M., Sc.D., LL.D., and others. 10th ed. (Pp. 991. 50s.) London: H. K. Lewis. 1948.

A textbook for the medical practitioner.

Textbook of Genito-Urinary Surgery. Edited by H. P. Winsbury-White, M.B., Ch.B., F.R.C.S. (Pp. 1,046. 90s.) Edinburgh: E. and S. Livingstone. 1948.

An illustrated textbook including operative details.

Post-Mortem Appearances. By J. M. Ross, M.D., B.S., M.R.C.S., L.R.C.P. 5th ed. (Pp. 308. 8s. 6d.) London: Geoffrey Cumberlege. 1948.

A short account for students and practitioners.

Recent Advances in Therapeutics. By J. R. Goyal, M.B., B.S. 3rd ed. (Pp. 288. Rs. 7.8.) Delhi: Yugantar Press. 1948.

A practical summary of recent advances.

Vision and the Eye. By M. H. Pirenne, D.Sc., Ph.D. (Pp. 187. 12s. 6d.) London: Pilot Press. 1948.

A short account of the structure and function of the eyes, including discussion of colour vision.

Handbook of Medicine for Final Year Students. By G. F. Walker, M.D., M.R.C.P. 4th ed. (Pp. 305. 25s.) London: Sylviro Publications. 1948.

A Short Practice of Surgery. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.I.C.S., F.R.S.Ed., and R. J. McNeill Love, M.S., F.R.C.S., F.A.C.S., F.I.C.S. 8th ed. Part II. (Pp. 420. Complete set 52s. 6d.) London: H. K. Lewis. 1948.

This part is on the surgery of the alimentary system.

On Life and Sex. By Havelock Ellis. (Pp. 282. 17s. 6d.) London: Wm. Heinemann. 1948.

Essays on the problems of sex in society.

Therapeutic Social Clubs. Edited by J. Bierer, M.D. (Pp. 73. 6s.) London: H. K. Lewis. 1948.

Articles by various authors on clubs for psychotic and neurotic patients, for the mentally defective, and for difficult children.

Educational Sociology. By F. J. Brown. (Pp. 626. 21s.) London: Technical Press. 1948.

A textbook of the sociology and psychology of education.

Proteins and Life. By M. V. Tracey, M.A. (Pp. 154. 10s. 6d.) London: Pilot Press. 1948.

An account of the structure and functions of proteins for the general reader.

A-B-C's of Sulfonamide and Antibiotic Therapy. By P. H. Long, M.D., F.R.C.P. (Pp. 231. 17s. 6d.) London: W. B. Saunders. 1948.

A concise summary of the use of sulphonamides and antibiotics.

New Biology. Edited by M. L. Johnson and M. Abercrombie. (Pp. 130. 1s. 6d.) London: Penguin. 1948.

Articles for the non-specialist on recent biological advances.

Nursing Arts. By M. L. Montag, A.M., R.N., and M. Filson, A.M., R.N. (Pp. 603. 17s. 6d.) London: W. B. Saunders. 1948.

An introduction to nursing for students.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 6 1948

CHEMOTHERAPY OF CANCER

From the work of Fildes and Woods in 1940 emerged the "rational approach" to chemotherapy. The administration of the sulphonamides starves susceptible bacteria of *p*-aminobenzoic acid, which is essential to their metabolism; from this it was an easy step to suggest that analogues of known bacterial growth factors or essential metabolites should prevent or slow down the growth of micro-organisms and might prove to be of considerable value as chemotherapeutic agents. Several hundred analogues of compounds known to be of importance to the cell have now been synthesized, and many of them interfere with the growth of bacteria *in vitro*. To give one example, vitamin K, 2-methyl-1,4-naphthoquinone, is an essential growth factor for certain fungi such as *Fusarium solani*. An active fungicide, 2-methoxy-1,4-naphthoquinone, was obtained from *Impatiens balsamina* by Little and his colleagues.[1] Its fungicidal action is due to the fact that it is a competitive inhibitor of vitamin K. Similar competition occurs between vitamin K and 2-chloro-1,4-naphthoquinone, the latter compound also acting as a fungicide.[2]

Many of the analogues which are active *in vitro*, however, are inactive *in vivo* or are too toxic to the host to be considered as possible chemotherapeutic agents. Only certain analogues of pantothenic acid, which is essential for the growth of some bacteria and the malarial plasmodia, retain the capacity to inhibit the growth of the same micro-organisms *in vivo* and at the same time fulfil the other requirements of a chemotherapeutic drug. Had not other antimalarial drugs such as chloroquine and "paludrine" been discovered during the war years it is probable that phenylpantothenone would be regarded as a considerable practical achievement for the "rational approach." Nevertheless, Sir Paul Fildes,[3] in opening a discussion at the Royal Society in June, expressed disappointment that this approach had yielded nothing of immediate chemotherapeutic value. This failure was attributed partly to the fact that the metabolic patterns of host and parasite were often so similar that an agent which interferes with a given process in one cell is only too likely to interfere with the metabolism of another cell, independent of species. The repetition of metabolic patterns is strikingly shown in the group of vitamins which make up the B complex. Members of this group have an extremely wide distribution as essential metabolites and are necessary for the nutrition of organisms as dissimilar as man and virus. Although analogues of the B vitamins have been synthesized in considerable numbers they have not found a place in chemotherapy because they interfere with the same fundamental processes in both parasite and host. Only *p*-aminobenzoic acid has been used clinically for its chemotherapeutic effect: its action on pathogenic rickettsiae was discovered when it was found that sulphonamides, which are normally inhibited by *p*-aminobenzoic acid, promote the growth of rickettsiae. Analogues such as those of aneurin, nicotinic acid, and folic acid have in fact produced in laboratory animals syndromes indistinguishable from those produced by simple dietary deficiencies.

Despite many failures in the use of these analogues for the treatment of infections a very striking application has now been found for them in the chemotherapy of the Rous sarcoma in chickens. Little and his colleagues[4] showed that by maintaining baby chicks on a diet completely lacking in folic acid (pteroylglutamic acid) the development of the Rous sarcoma could be prevented in 100% of them, and in 40% of six-weeks-old birds. On the other hand, N-methyl folic acid, pteroyldiglutamic acid, and pteroyltriglutamic acid can all replace folic acid, since the growth of tumours is not prevented in birds fed on a diet free from folic acid and then injected with any of these compounds. If, however, folic acid was injected with *d*(−) glutamic acid, pteroylaspartic acid, pteroic acid, N-methylpteroic acid, or P.A.B.-triglutamic acid no tumours developed, since these compounds were unable to replace folic acid. The next step was to feed chickens on an ordinary mixed diet and to determine the effect on the development of the Rous sarcoma of known analogues of folic acid. When injected into chickens in doses of 200 or 400 μg. per day 4-amino-pteroylaspartic acid was found to reduce the number of chickens developing tumours by 60%. When 4-amino-folic acid with *d*(−) glutamic acid was used in a dose of 400 μg. per day results were even more striking, for the development of all tumours was prevented; with a daily dose of 200 μg. only half the birds developed tumours.

These findings are of very considerable interest. It is now four years since Leuchtenberger and his colleagues[5] first claimed that pteroyltriglutamic acid, the original *Lactobacillus casei* factor, inhibited the growth of sarcoma 180 transplanted in female mice. In later publications[6] they showed that folic acid itself had no therapeutic effect on spontaneous breast tumours in mice, whereas the fermentation *L. casei* factor caused complete regression in 30–40% of tumours.

These findings served as an impetus to the synthesis and to the clinical use of pteroyltriglutamic acid, now referred to as teropterin. This is a yellow powder, freely soluble in normal saline, apparently stable at room temperature, and completely painless on injection. No toxic effects have been observed in animals. More than 100 cases of malignant growths in man have been treated with this drug in Boston, and details of 20 patients who have received the drug in New York have now been reported by Lehr and his colleagues.[7] These patients, in an advanced state of the disease, have been under treatment for one to three

[1] *J. biol. Chem.*, 1948, **174**, 335.
[2] Guerillot-Vinet, J., and Guerillot-Vinet, M., *C. R. Acad. Sci., Paris*, 1948, **227**, 93.
[3] *Nature*, 1948, **162**, 356.
[4] *Trans. N.Y. Acad. Sci.*, 1948, **10**, 91.
[5] *Proc. Soc. exp. Biol., N.Y.*, 1944, **55**, 204.
[6] *Science*, 1945, **101**, 46, and ibid., 1946, **104**, 436.
[7] *Trans. N.Y. Acad. Sci.*, 1948, **10**, 75.
[8] Ibid., 1948, **10**, 71.
[9] Ibid., 1948, **10**, 99.

months. In the majority of cases pain was relieved, and the patients became more cheerful and mentally alert. Some put on weight and have returned to work. Klainer[8] reports a striking improvement in a female patient with metastases in the spine secondary to a breast tumour which had been removed. She was given 150 mg. of testosterone propionate daily in three divided doses and 60 mg. of teropterin, each drug being injected intramuscularly. After nine months, still on teropterin, the patient was completely ambulatory. Radiographs of the spine showed regeneration of bone in the involved areas, and her only complaint was of mild aching in the lumbar spine after prolonged walking or standing. How far improvement was due to teropterin and how far to testosterone cannot yet be judged.

Teropterin has also been used by Meyer[9] in the treatment of leukaemia. In chronic lymphatic leukaemia no striking changes occurred with doses up to 200 mg. a day. Subjective improvement was seen in two patients with myelomatosis, but no changes were found in the bone marrow. In cases of acute lymphoblastic leukaemia both teropterin and pteroyldiglutamic acid have reduced the white cell count. Improvement has also been observed in patients with acute myelogenous leukaemia treated with N-[4-([(2-amino-4-hydroxy-6-pteridyl)methyl] amino)-benzoyl]*dl*-aspartic acid or 4-(-N[(2-amino-4-hydroxy-6-pteridyl)-methyl]-N-methylamino)benzoic acid. Both these compounds are said to act as folic acid antagonists. While no claim can be made that the rational approach to chemotherapy has yet provided a cure for human malignant disease, folic acid antagonists form a group of compounds which will well repay further intensive investigation.

VITAMIN C

The daily amount of vitamin C required by man for health, the earliest clinical signs of deficiency, and the effects of a deficiency upon the healing of wounds are questions which a recent large-scale experiment was designed to answer. The results are contained in the preliminary report[1] of the Vitamin C Subcommittee of the Accessory Food Factors Committee of the Medical Research Council. The experiment, which continued for eighteen months, was carried out at the Sorby Research Institute of the University of Sheffield under the supervision of Professor H. A. Krebs. Twenty volunteers took part and between them submitted to 72 wounds. The experiment was a "blind" one in that neither observed nor observer was allowed to know whether any particular individual was deprived or protected—an essential requirement when clinical features are to be assessed. The diet was designed to be complete, well balanced, and relatively palatable, but it contained less than 1 mg. of irremovable vitamin C. This vitamin was provided in tablet form, and after a preliminary period of saturation (70 mg. per day for six weeks) dummy tablets identical in size, shape, and taste were substituted. Three control subjects continued to receive 70 mg. per day; seven received 10 mg. per day, whilst the 10 remaining were completely deprived of the vitamin apart from the irremovable milligramme (or less). All these 10 developed symptoms of scurvy. Four of those in the group restricted to 10 mg. per day remained normal during the whole period (424 days in three cases and 252 in the fourth). In the three others there were no signs of scurvy after 160 days, and they were then totally deprived of the vitamin in order to find out whether the period of low intake had rendered them more susceptible. In two of these three a period of total deprivation for 71 days produced at most doubtful initial lesions (slight hyperkeratosis).

In order to determine the minimum effective curative dose six of the totally deprived who had developed clinical scurvy were given 10 mg. of vitamin C per day; they steadily improved upon this very small dose. Some tests for physical fatigue, though not conclusive, showed small differences in favour of the group receiving 70 mg. compared with those on 10 mg. per day. There are thus good reasons for supposing that 10–11 mg. is the minimum daily requirement for the human adult, but the subcommittee considered that it would not be unreasonable to recommend 30 mg. as the daily requirement, since a margin of safety must be allowed for additional needs as yet very ill-defined. It is, however, obvious that intakes much less than this are not necessarily detrimental to health. The U.S. National Research Council's[2] figure of 75 mg. was based upon saturation experiments and theoretical considerations, and there is no evidence to show that it has any advantage over 30 mg., which was the amount recommended by the League of Nations Technical Commission on Nutrition.[3]

When the records of the experiment were reviewed the earliest clinical sign of deficiency was found to be hyperkeratosis of the hair follicles. It occurred after 17–21 weeks, but it is not diagnostic of scurvy. The perifollicular haemorrhages which followed (at 26–34 weeks) are almost diagnostic. Swelling and haemorrhages of the gums appeared later (30–38 weeks) and less constantly; this seems to indicate that oral lesions should not be diagnosed as scurvy in the absence of skin lesions, unless hard ship's biscuit happened to be the main item of food. An interesting sign was a striking exacerbation of previously existing acne; this was noticed after 22 weeks. The volunteers were intelligent, fully co-operative, and under skilled psychiatric observation, yet it proved impossible to differentiate the deprived from the protected by subjective symptoms or psychological abnormalities. Tests specially designed to detect the apathy which is alleged to accompany scurvy gave negative results. There were no complaints of general pains or weakness. There is thus no experimental basis for the treatment of vague subjective symptoms by vitamin C.

Much biochemical information was acquired. The vitamin-C content of the blood plasma in the totally deprived group and also in those limited to 10 mg. of the vitamin per day fell rapidly, but it proved practically impossible to decide from a single plasma test whether any particular individual was upon a fully protecting dose of 10 mg. or totally deprived of the vitamin and either suffering from scurvy or in imminent danger of developing it. The estimation of vitamin C in the white corpuscles proved to be

[1] *Lancet*, 1948, **1**, 853.
[2] *Repr. nat. Res. Coun. Wash.*, 1943, No. 122.
[3] *Quart. Bull. Hlth Org. L.o.N.*, 1938, **7**, 461.

a more sensitive test, and there is hope that improvements in technique may make it possible to estimate accurately the vitamin-C deficiency in any individual. At present, however, the test can be used only to exclude the diagnosis of scurvy. No abnormalities were observed in the capillary filtration rate, in the body weight, in the incidence of minor infections, in the appearance of the capillaries of the nail bed and of the conjunctivae, and in the dark-adaptation of vision. There were no haemorrhages apart from those in the skin or gums. The "cuff" tests for capillary fragility gave no consistent results. Haemoglobin estimations and erythrocyte and leucocyte counts, including differential counts, were normal and thus gave no support for the theory that vitamin C is a necessary factor in haematopoiesis. Platelets, bleeding time, plasma protein, albumin-globulin ratio, blood urea, and phosphatase were all normal.

These hard facts will disprove some of the suggestions which have been made about the clinical and pathological signs of vitamin-C deficiency, but they will not obscure the fact that scurvy can be a dangerous condition. Three out of ten of the deprived subjects developed serious symptoms. The most severely affected of these suffered an exacerbation of a previously existing but symptomatically latent tuberculous spondylitis; another had an acute cardiac emergency with an E.C.G. suggestive of coronary thrombosis; whilst the third had praecordial pain associated with heart-block (partial) not discovered in a previous E.C.G. All had recognizable scurvy at the time of the breakdown. The effects of vitamin-C deprivation on wound healing are more difficult to assess from the report, and it is to be hoped that fuller details will be published. The old observation that scars become red and livid was confirmed. It was established that when clinical signs of scurvy were present wounds often showed defects of healing, but in one individual suffering from scurvy a wound healed normally. In the group of subjects taking 10 mg. of the vitamin per day no defects of wound healing were seen.

It would be almost impossible in this country to provide throughout the year enough vitamin C to meet the recommended American daily requirement of 75 mg., and it is satisfactory that the subcommittee found that such a large amount was not necessary for health. It is extremely improbable that any individual living in this country on the present rations can be in danger from vitamin-C deprivation. The available supplies of the vitamin can be best used by treating vigorously the real cases of scurvy so as to obtain rapid recovery; they should not be frittered away in treating a multitude of indefinite symptoms classified as "preclinical" scurvy. It is significant that the clinical observers were seriously concerned about the condition of at least one of the volunteers during the acute cardiac emergency which followed a few hours after an agility test. It seems clear that any patient diagnosed as suffering from scurvy should be admitted to hospital and saturated with ascorbic acid as soon as possible. Some physicians might feel inclined to try out the curative effect of small doses in order to confirm the findings of this report, but such an experiment should be undertaken only with a full sense of the responsibility incurred, for liability to sudden death during the course of the disease was formerly well recognized. When the full report is published it will undoubtedly be a unique contribution to the literature on the subject, and the M.R.C. is to be congratulated on providing the organization and funds which made the research possible.

SURGICAL TREATMENT OF MENIERE'S DISEASE

Perhaps only those who have suffered from severe attacks of vertigo can realize their devastating effects, social and economic. Ménière's disease is probably the commonest cause of this disability, and treatment is within the province of both physicians and surgeons. Physicians claim that medical treatment can effect a cure, but whether this treatment takes the form of limitation of intake of water or of salt, of injections of antihistamine substances, or of the administration of drugs the results are by no means permanent and some are not appreciated by the patient. Surgeons have therefore applied themselves to the problem. In view of Charcot's statement in 1874 that vertigo ceased when deafness became absolute it appeared that section of the eighth nerve should cure the vertigo, and this was suggested by Ballance in 1894 and performed by Frazier[1] in 1904.

Since this date neurosurgeons have developed the operation of intracranial section of the nerve. In 1933 Dandy[2] described the results of section of the vestibular portion without division of the cochlear nerve; this cured the vertigo and left the hearing unaffected. This operation was adopted by many neurosurgeons with very good results, though it is not without risk to life. Ray[3] has recently advised section of the whole nerve, since he found that even if a few fibres of the vestibular portion are overlooked vertigo can persist. As most patients are deaf before operation, he believes that the subsequent complete deafness does not disturb them.

Otologists have devised operations to deal with the labyrinth itself, directly or indirectly. Long before Hallpike[4] demonstrated dilatation of the endolymph system in cases of Ménière's disease this condition was suspected, and operations were performed to diminish pressure in the internal ear. The earliest was lumbar puncture, and later drainage of the pontine cisterna was undertaken. In 1927 Portmann[5] opened the saccus endolymphaticus, and this gave successful results in a considerable proportion of cases. Direct drainage by opening the external semicircular canal was performed by Hautant; this procedure, combined with injection of absolute alcohol to destroy the function of the labyrinth, was advocated by Mollison.[6] Injection of alcohol through the footplate of the stapes was devised by Wright. All these operations had the disadvantage of destroying hearing. Later Cawthorne[7] opened the external canal by a specialized technique and removed the membranous canal; this cures the vertigo without affecting the hearing.

In a paper appearing elsewhere in this issue Mr. E. R. Garnett Passe and Dr. J. S. Seymour approach the problem from a different standpoint. They put forward a vascular cause to explain the hydrops of the labyrinth, and suggest that differences in the blood supply to different parts of the internal ear may well account for the relative differences between deafness and vertigo; in some cases vertigo is the important symptom, in others deafness. Since the vertebral

[1] *N.Y. St. J. Med.*, 1905, **81**, 272, 332.
[2] *Amer. J. Surg.*, 1933, **20**, 693.
[3] Ibid., 1948, **75**, 159.
[4] *J. Laryng.*, 1938, **53**, 625.
[5] Ibid., 1927, **42**, 809.
[6] *Acta Oto-laryng., Stockh.*, 1939, **27**, 222.
[7] *J. Laryng.*, 1943, **58**, 363.

artery supplies the internal ear, they approach the vessel through the subclavian triangle, and after dividing or stripping it they excise the stellate ganglion. Of the 12 cases operated upon all were relieved of vertigo; in all but one hearing was improved; and in nine the tinnitus was modified or relieved. This is only a small number from which to draw final conclusions, but the results are encouraging.

TREATMENT OF ACTINOMYCOSIS

The treatment of actinomycosis, as of many bacterial infections, has twice been improved in recent years. Whatever view may be taken about the action of iodine in this disease it is generally conceded that the sulphonamides have a more pronounced and dependable effect. Penicillin proved to be even more efficacious and often actually curative. Decker[1] reviewed the earlier results of penicillin treatment and also discussed other forms of treatment. He described three cases typifying his own past experience with this disease: one was cured with penicillin, one uncured by iodine, and one was not diagnosed until the post-mortem examination. It seems probable that cases of actinomycosis still remain undiagnosed or are recognized at so late a stage as greatly to reduce the chances of successful treatment. Both the clinician and bacteriologist should never lose sight of the possibility of this infection in connexion with lesions of the jaw, ileo-caecal region, and particularly of the lung, pleura, and chest wall. It is in the thorax that the disease is likely to extend furthest without recognition.

Although the anaerobic *Actinomyces* usually responsible for human infections has been recognized as penicillin-sensitive for some years, there is evidence that the degree of sensitivity varies and that this may affect the results of treatment. Owing to the slow growth of the organism and the difficulty of preparing a standard inoculum estimations of sensitivity can only be approximate, and all existing information on this subject requires review in the light of Holm's[2] studies, which are the most thorough hitherto made. He worked with 29 strains derived from 27 patients and determined their sensitivity to penicillin by cultivation in a liquid medium containing falling concentrations of the drug, controlling the test with an identical series inoculated with a standard staphylococcus. The inoculum used was of two kinds, either a suspension obtained by crushing a colony between two sterile slides or a whole colony. When suspensions were used, all the strains were found to have approximately the same sensitivity as the control staphylococcus. On the other hand, entire colonies of the majority of the strains were able to grow in considerably higher concentrations of penicillin—3 of them in 1 unit per ml., the highest concentration tested. By using colonies of different ages Holm demonstrated that resistance varied with colony size. Comparative tests with whole colonies and suspensions equivalent in quantity showed that this was due not just to the bulk of the inoculum, since the suspensions were more readily inhibited. This difference in result according to the dispersion of the inoculum was observed in a group of 20 typical strains. A smaller group differing in morphology, colonial characters, and in being CO_2-sensitive did not behave in the same way. As Holm points out, the response of the disease to treatment will depend on the capacity of penicillin to attack the organism in the form in which it exists in the lesions, and a sensitivity test using whole colonies as the inoculum is therefore the better guide. The fairly high degree of resistance of some strains when tested in this way may be the explanation for the lack of response to penicillin in some cases. Patients infected with these strains require a larger dose for a longer time. Perhaps the only safe policy is to give large doses in all cases of actinomycosis unless or until the strain of *Actinomyces* can be examined by Holm's technique, a procedure calling for both time and skill. Thus to discuss the uses of chemotherapy in this disease is not to imply that it can replace surgery: drainage is essential, and excision, if feasible, is perhaps the most valuable measure of all.

[1] *J. thorac. Surg.*, 1946, **15**, 430.
[2] *Acta path. microbiol. scand.*, 1948, **25**, 376.

JET INJECTION

A new method of injecting drugs without either syringe or needle is based on the fact that an extremely fine high-pressure jet of liquid can pierce the skin without producing pain. Hingson and Hughes[1] have described the apparatus required. The material for injection is contained in a small sterile metal ampoule shaped like a blunt-nosed bullet, with a hole about three-thousandths of an inch in diameter in its end. The ampoule, which is encased in an aluminium container to avoid contamination, is locked in the front of the instrument. This is shaped like the case of a large electric torch and contains a calibrated high-tension spring controlled by a release button. When the spring is released it propels a plunger against the metal ampoule, from which liquid is forced through the minute opening as a fine high-velocity jet under pressures varying from 2,300–3,500 lb. per sq. in. (1,000–1,600 kg. per 6.45 cm.^{2}). The injection is given by placing the blunt nose of the metal ampoule against the skin, which is stretched taut, and then releasing the spring. The jet which is forced out passes through the skin to a depth of 0.2–2 cm. according to the site of injection and the texture of the patient's skin and tissues.

The advantages claimed for jet injection are complete freedom from pain in most patients and a considerable saving of time, since the ampoules are supplied already sterilized. There is obviously a use for such a device in clinics where many injections are given, as in immunization clinics, and perhaps diabetics and those receiving penicillin or streptomycin injections several times a day would prefer it to the hypodermic needle. Jet injection, however, has its drawbacks: if the skin is wet, or if the nose of the ampoule is not in close contact with it, or is tilted, the injection produces a cut and sometimes a blister. It cannot be used for carefully placed injections or for the injection of oily liquids. It is also possible that nerves and blood vessels near the skin might be injured by a high-pressure jet. Perhaps the greatest drawback at present is the cost of the apparatus. Jet injection is, however, the first basic change in injection technique for nearly a hundred years. It has already been tried out in the U.S.A. in V.D. and tuberculosis clinics for the routine injection of penicillin and streptomycin.[2 3]

[1] *Curr. Res. Anesth.*, 1947, **26**, 221.
[2] Hingson, R. A., and others, *J. vener. Dis. Inform.*, 1948, **29**, 61.
[3] Hirsch, H. L., and others, *J. Lab. clin. Med.*, 1948, **33**, 805.

The Thomas Vicary Lecture entitled "The Portraiture of William Harvey" will be delivered by Mr. Geoffrey Keynes before the Royal College of Surgeons of England (Lincoln's Inn Fields, London, W.C.) on Wednesday, Nov. 17, at 5 p.m.

The Mitchell Lecture will be delivered by Dr. Robert Coope, F.R.C.P., before the Royal College of Physicians of London (Pall Mall East, S.W.) on Thursday, Nov. 18, at 5 p.m. His subject is "Tuberculous Enlargement of Intrathoracic Lymph Nodes and its Aftermath."

STREPTOMYCIN

THE PRESENT POSITION

A meeting of the Medical Society of London was held on Oct. 25 for a discussion on streptomycin. Dr. JENNER HOSKIN presided.

Dr. JACK RUBIE gave a brief account of the treatment at Highgate Hospital by means of streptomycin of a group of cases of children with tuberculous meningitis. The scheme of treatment was as follows:

	Days
Intramuscular and intrathecal injection	28
Intramuscular only	28
Intramuscular and intrathecal	28
Rest	28
Intramuscular only	28

Followed by observation for two months or more, with further treatment if symptoms reappeared.

The daily dose intrathecally was 0.1 g. in 10 ml. solution, and intramuscularly 0.02 g. per lb. body weight. Some of the cases under treatment showed symptoms such as fever, anorexia, vomiting, and skin rashes, but these, if at all severe and prolonged, were considered more likely to be due to the disease than to the drug. Two types of skin lesion were encountered: an urticarial eruption and an exfoliative dermatitis. The latter responded remarkably well to a local application of cod-liver oil. Ten of the cases were operated on to relieve hydrocephalus. It was difficult to give the indications for this operation, but so far it had been performed when there was a suggestion of relapse with headache, vomiting, and papilloedema. The puncture was made to approach the descending horn of the lateral ventricle, and a tube was inserted into the ventricle and allowed to drain. This was carried out as a prophylactic measure in children under 3. The lumbar puncture was continued for the streptomycin administration, and the operation used only for the purpose of mechanical drainage.

In a small number of cases sulphetrone had been added to the streptomycin. This was given only intrathecally, and its diffusion into the blood by that route gave almost as high a blood level as by the intramuscular route. This drug was toxic at anything above the blood level of 10 or 12 mg. per 100 ml. One case which had received this combined treatment had a normal cerebrospinal fluid 100 days from starting treatment, and a second case appeared to be doing well. In nursing these patients it was important, especially with those under 3 years of age, that they should not lie supine for long periods. The children were made to sit up and were kept on the move, and thus exudate was prevented from forming as a solid plaque in the posterior fossa.

Of 58 patients 22 had survived more than 120 days and 20 were doing well. Out of this number 44 had had the combined intramuscular and intrathecal treatment, and of these 19 were alive after 120 days and 17 were doing well; 10 had had intramuscular treatment alone, and among these there were only two survivors; and four others started with intramuscular treatment, but when it was realized that this was not proving efficacious they were switched over to intrathecal treatment, and of these only one survived. He emphasized the improved results in early cases: out of 17 cases in which treatment was begun early 11 had survived. Dr. Rubie showed photographs of a number of these children, to all appearances normal, who, he said, had been under observation for varying periods up to sixteen months; 12 of them now had a normal cerebrospinal fluid.

Pulmonary Tuberculosis

Dr. GEOFFREY MARSHALL referred to the Medical Research Council committee which was set up two years ago. [The committee's report appeared in full in the *British Medical Journal* of Oct. 30, p. 769.] Dr. Marshall said that tuberculous meningitis presented itself most obviously as a condition in which the remedy should be tried, because the death rate was so nearly 100% that any good results in such cases must indicate that streptomycin had value, as indeed had been proved. On the other hand, in tuberculous disease of the lung it was much more difficult to assess the results of treatment, and it was necessary to have control cases. The 55 patients who received streptomycin were given treatment on what later experience showed to be a rather massive scale—0.5 g. of streptomycin four times in twenty-four hours. He believed that 1 g. a day was sufficient.

The overriding difficulty in the streptomycin treatment of pulmonary tuberculosis had been the development of resistant strains of tubercle bacilli. This difficulty did not arise in the cases of tuberculous meningitis. If with the development of resistance something like, say, ten times as much streptomycin was required as when treatment first started it might not worry them, but within about six or eight weeks many strains of tubercle bacilli were found in the sputum which called for about a thousand times the original strength of streptomycin. As the strains became more resistant not only was the lessened effect demonstrable bacteriologically, but parallel with it was a decline in the clinical results. The patients were better at the end of three months than they were at the end of six. Some attempt had been made to "dodge" this effect by altering the rhythm of treatment. During the first month relatively little resistance was found and during the second month much more, so that they thought of giving streptomycin for a month and then desisting for a month. Unfortunately this did not work. During the second month, even if the streptomycin was discontinued, the resistant strains increased. Perhaps it was better to give streptomycin for six weeks and then end it. It was a valuable remedy, but it must be used with discretion and not in pulmonary tuberculosis unless there was a real indication for it.

Many patients who were bad risks, coughing up large numbers of tubercle bacilli, had done so well that it was possible to institute collapse therapy within six months, whereas this had not been advisable at the beginning. Tuberculous ulceration of the bronchi had healed completely under streptomycin, but the difficulty arising from cicatrization remained. A small number of cases of acute miliary tuberculosis had recovered. Toxic reactions took the form of urticaria and other forms of rash, and occasionally there was damage to vestibular function, in some cases permanent, and affecting the middle-aged and elderly rather than the young.

Bact. coli Infections

Sir ALEXANDER FLEMING said that under treatment with streptomycin patients with miliary tuberculosis got well for a time, but the disease returned. It might not be so great a misfortune that the supply of streptomycin was restricted; when supplies became more abundant, as they would, there might well be misuse and disappointment. Streptomycin had a powerful effect on *Bact. coli*. The results within twenty-four hours in some infections were marvellous, but if the infection did not disappear within twenty-four or forty-eight hours the chances were that the *Bact. coli* had become resistant. There was either a quick result or no result at all. It was a pity to tinker with the drug, and it was just as well in these *Bact. coli* cases to give as big a dose as practicable and kill off the organism. Certain results indicated that given by the mouth streptomycin had a rapid effect in infantile diarrhoea. It was a local action: no big dose need be given. This might turn out to be a very important use for this drug.

Dr. JOSEPH SMART said that streptomycin should be used with great care and under certain specified conditions. It was thought that it might be useful to administer by inhalation and placing the drug directly on the larynx, but this had proved disappointing. On the other hand, a tuberculous larynx treated with streptomycin intramuscularly responded very well. Cases of gross ulceration and massive destruction of the main bronchi were relatively rare, but it was quite common to get small superficial ulcers, and under streptomycin treatment such ulcers healed very well.

Urinary Infections

Mr. E. W. RICHES spoke of the use of streptomycin in tuberculous infections of the urinary tract. With the small amounts available it had not been possible to try it extensively. He had used it, however, in a number of cases which he would describe as complicated in the sense that they had some other surgical condition as well as the infection; they were cases

which had undergone prostatectomy or had stricture, and so on. In these cases they had concentrated on organisms which were not responsive to most other drugs, particularly *Ps. pyocyanea*. They had given doses of 3 g. a day, up to a total of 12 g. *Ps. pyocyanea* had disappeared in 14 out of 20 cases; *B. proteus* in 4 out of 4; *Bact. coli* was not always eliminated. The good results did not mean that the urine was always sterile, because frequently at the end of treatment there were streptomycin-resistant organisms left. He did not think that the results of treatment should be assessed solely on the basis of the bacteriological picture. There had been a number of cases in which the clinical improvement had been most striking. It was not to be expected that a permanent sterilization of the urine would be obtained with streptomycin in the presence of any surgical lesion such as urinary obstruction, or in gross organic disease. The great value of streptomycin urologically was in post-operative or more particularly post-radiation infections. In cases such as carcinoma of the bladder treated with radium a *Ps. pyocyanea* or *B. proteus* infection might in the ordinary way go on for months, and in such cases streptomycin was of great value. In urinary tuberculosis there had been no proved cases of permanent disappearance of tubercle bacilli from the urine, but a certain amount of clinical improvement had been observed, as shown by increased capacity of the bladder.

Dr. W. G. OAKLEY said that in treating by means of streptomycin diabetic patients with urinary infection it was important to get rid of the sugar before giving the drug. Dr. BUTLER described a case of *Bact. coli* infection in the urine with synovitis, both of which conditions cleared up under a total of 12 g. of streptomycin.

Dr. MARSHALL, in reply, said that it was the general experience that little was seen of resistant strains in treating cases of meningitis, but such resistance was almost invariable in pulmonary tuberculosis. To show the value of streptomycin in ulcerative conditions he mentioned the case of a woman who became pregnant. The tuberculosis officer advised termination of pregnancy. The woman belonged to a Church which frowned upon that procedure, and she went from bad to worse. After the birth of the child she developed a severe ulceration of the epiglottis, so that she could not swallow even saliva. A supply of streptomycin was obtained, and within five days of starting treatment she was perfectly comfortable, and within a few weeks the ulceration of the epiglottis had healed.

THE PRACTITIONER'S PART IN THE ANTI-TUBERCULOSIS SCHEME

A PLEA FOR PROMPT RADIOGRAPHY

BY

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There is in this country a widespread failure to tackle tuberculosis adequately, and it is the aim of this article to deal shortly with one vital aspect of the problem. Through no fault of his own the general practitioner in particular does not at present fully utilize his unique opportunities of raising the Tuberculosis Service from its present mediocrity to the highly efficient organization that it might and should be. It will be shown that avoidable delay in the diagnosis of pulmonary tuberculosis occurs in the doctor's surgery, and the significance of this will be indicated. The practitioner will then appreciate how indispensable is his co-operation and how best to use his opportunities of attaining early diagnosis.

Delay in Diagnosis

It was decided to investigate the histories of a series of cases to determine what period of time constituted the average delay in diagnosis and, if possible, to discover where the greatest delay occurred. For this purpose 345 consecutive cases were taken, diagnosed in the years 1946 and 1947 and resident in the area of North-West London administered by Willesden Chest Clinic. Of these cases 297 were referred to the chest clinic for investigation by their own doctors on account of symptoms. Of the 48 cases referred from a mass radiography unit 35 so far have proved inactive and symptomless, and of 13 which proved active 10 had symptoms. The first obvious fact arising from these figures is that *99% of the active cases in this series had symptoms for varying periods of time before attending the chest clinic and could therefore have been diagnosed earlier had action been taken immediately these had begun.*

The histories of the patients who had consulted their own doctors (86%) were further analysed to discover (*a*) the time interval between the first suggestive symptom and first seeking medical advice, (*b*) the time elapsing after this first consultation before the patient's chest was *x*-rayed. The intervals in individual cases vary widely, but the average figures for the whole series are as follows:

First symptoms to first consultation	1.7	months
First consultation to diagnostic *x* ray	4.0	,,
Total	5.7	,,

The immediately striking fact is not only the length of delay but that over two-thirds of this delay occurs after the patient has reported symptoms to his doctor. Furthermore, it is not only patients with relatively minor symptoms whose disease is missed: in 56% of practitioners' cases in this series there was a delay of over four weeks in spite of the patients reporting haemoptysis, severe chest pain, or cough lasting more than one month.

It is instructive to compare these figures with those given by Mann (1943) for a group of sanatorium patients:

Delay in consulting doctor	3.64	months
Delay before referred for consultation	3.28	,,
Total	6.92	,,

The difference between the two series of figures is so marked that a conclusion is probably justifiable in spite of their not being strictly comparable (the present figures refer to a chest clinic; Mann's to a sanatorium). The significant fact will immediately be appreciated: although the patient's delay in attending a doctor's surgery is markedly less in this series, *there has been no similar shortening of the period between the patient's first visit and a diagnosis being attained.* It would appear that the general public is becoming more conscious of the significance of pulmonary symptoms and the necessity for *x*-ray examination, thus throwing into relief the deplorable fact that a similar event is not occurring in the ranks of our own profession.

Significance of Delay

Although pulmonary tuberculosis forms our major public health problem to-day, the methods for its control are deplorably inadequate. The disease accounts for more deaths in the productively useful age group than any other single factor just at a time when an increase of industrial output is urgently required. It is widely recognized that the earlier in the evolution of the disease treatment is instituted the rosier is the outlook for the individual sufferer, yet *the wait for sanatorium admission is in the region of six to nine months.* The rise in the tuberculosis death rate in 1947 (*Lancet*, 1948) is probably in part a reflection of this fact. What is not so well appreciated is that the majority of dangerous infections start acutely in young adults and may progress very rapidly indeed. Weeks or even days of delay in referring a patient for chest radiology are often of vital significance, whilst the months indicated by these figures often mean that the patient is beyond treatment before his name can even be added to the bottom of the sanatorium waiting-list.

I believe that the main reason for the failure to utilize even existing facilities for radiology is the widespread misunderstanding of the symptomatology of incipient tuberculosis. Sir James Mackenzie (1923) wrote, "The defective education of the general practitioner renders him incapable of utilizing his opportunities for the progress of medicine," and I would add that extreme overwork too often exaggerates this position. Unfortunately both textbooks and the propaganda accompanying

the mass miniature-radiography campaign tend to suggest that insidious onset is the rule, so that the practitioner may even be led to believe that early diagnosis is a Utopian objective.

The figures given show that a definite symptomatology is present in practically every active case. Sometimes dramatic but frequently only slight, these symptoms may have to be diligently sought after, and unfortunately they are often suggestive of other less serious illnesses. Such mimicry may lull the practitioner into inactivity, while possible suspicions are further dispelled when the patient, after an illness of acute onset, appears to recover his former health wholly or in part (a common temporary occurrence). In addition physical signs may be absent or positively misleading. A statement made by Fishberg and quoted by Jessel (1941) is an apt ending to this short review : "There may be active phthisis without physical signs revealing themselves even to the best-trained specialist . . . but there is no active phthisis without constitutional symptoms."

The ultimate remedy obviously lies in improved and more realistic teaching of the subject in our medical schools, but meanwhile more immediate results *must* be obtained.

The Practitioner's Part

To obtain these immediate results is not difficult; every suspicious case should have chest radiology arranged *when first seen*. Leaving arrangements till a later date and "watching" the patient in the meantime is not adequate, for he may not return. To give practical help there is reproduced below the table (with slight additions) compiled by Toussaint (1946). The occurrence of any one of these symptoms or illnesses should lead to arrangements being made for immediate *x*-ray examination of the chest.

Cough, Haemoptysis, Dyspnoea, Laryngitis (Including senile patients)	Influenza out of season
Lassitude	Recurring febrile chills
Bronchial catarrh	P.U.O.
Pneumonia	Pleurisy, pleurodynia, or pain in chest
Ischio-rectal abscess	Loss of weight, Anorexia, Anaemia and debility, Amenorrhoea (unexplained) (Particularly females aged 15–30)
Erythema nodosum	
Phlyctenular conjunctivitis	

(The occurrence of meningeal, miliary, or other type of active primary tuberculosis in an infant is an added essential reason for radiological examination of adult contacts.)

It may be objected that without adequate bed accommodation for the tuberculous more frequent and early diagnosis will not improve our position. It is, however, only the early case that may be treated successfully at home—an alternative to the sanatorium which is bound to gain favour as the gratifyingly successful results now being obtained by pioneers in this field are appreciated. Toussaint, working in Bermondsey and Willesden, and Heller in Hounslow (personal communications), have found that domiciliary collapse therapy, initially undertaken as a necessity, has not only proved highly successful and enabled some patients to return to work before their sanatorium vacancy would have become available, but the waiting-list can in practice be almost ignored. A second criticism sometimes advanced is the suggestion that existing *x*-ray facilities would be inadequate to deal with the number of films needed. My only comment upon this is again to draw attention to the fact that even these existing facilities are not being fully utilized and to point out that the mass miniature-radiography units could be more profitably employed. Hopelessly inadequate for their present job, such machines are capable of going a long way to meet an increasing demand for chest radiography by practitioners.

Finally, it must be realized that the general practitioner service is the only really nation-wide network immediately available to advise the sufferer, and if he slips through this health sieve subsequent delay in diagnosis is inevitable. Time lost in a case of tuberculosis can never be regained, and only the practitioner has the never-repeated chance to act on the first complaint. The patient often looks fit; he may be well nourished and have no physical signs; but he has a history to relate or he would not have sought advice. *It is upon suggestive symptoms alone that prompt radiography must be ordered.*

"Resist beginnings; too late is the medicine prepared when the disease has gained strength by long delays."—OVID.

Summary

It is shown that serious delay is usual in the diagnosis of pulmonary tuberculosis—on the average a total of 5.7 months, of which *over two-thirds occurs in the doctor's surgery* (4 months). It is also shown that the common assumption that early tuberculosis is symptomless in the majority of cases is a fallacy: 99% of the active cases had symptoms for an average of 1.7 months before attending for consultation or radiography.

The great significance of this serious delay in diagnosis is stressed by reference to the present social importance of the disease, its rapidity of progression in the young adult, and the close correlation between prognosis and early diagnosis.

It is indicated that the general practitioner can materially improve this position by (*a*) realizing that incipient pulmonary tuberculosis has symptoms that may closely mimic other common and less significant illnesses, and that it may be impossible by physical examination alone to make a differential diagnosis; (*b*) above all, taking action in the shape of immediate reference for chest radiography in any case reporting the slightest symptoms. A table of symptoms is given as a guide to the type of case that should be so referred. Even existing radiological facilities are far from fully utilized.

Finally it is pointed out that if *early* cases are obtained they can be treated at once, in spite of the present bed position, if domiciliary collapse therapy is extended to more chest clinics. Practitioners therefore need not hesitate to proceed on the lines indicated. With their help the attack on tuberculosis could be highly successful: without it no other method can at present reap more than a small part of the possible harvest.

My grateful thanks are due to Dr. C. H. C. Toussaint, my former teacher and chief, for allowing me to investigate his cases whilst working at Willesden Chest Clinic. His inspired example and enthusiasm for early diagnosis led me to undertake this investigation.

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THE MEDICAL PROTECTION SOCIETY

Sir Ernest Rock Carling, presiding at the annual meeting of the Medical Protection Society on Sept. 29, said that it was not yet known what effect the transfer of the whole profession to the Ministry of Health would have upon litigation. The Society had had considerable experience in dealing with Government Departments, particularly the Services and the Treasury, and nothing in its past experience led it to expect that the profession would be less likely to be attacked by disgruntled patients in the future than in the past. One feature of the National Health Service might be of advantage. Medical men and dentists were obliged under the Act to keep records. Nothing had prejudiced a practitioner's case more in the courts than lack of record-keeping. Often the Society had been obliged to say that there was no defence owing to the absence of proper records. A great deal of trouble had been experienced over broken needles, and the Society had obtained reports from metallurgists which in all the cases submitted showed that there were manufacturing defects which it was impossible for the user to detect. One question which arose not infrequently was whether a practitioner should tell his patient or the patient's relatives of some mishap. It was conceivable that there were circumstances in which it was not good on medical grounds to tell the patient, but in the vast majority of cases it was important that the patient should be at once informed.

Dr. G. M. Stoker was introduced as the new chairman of council in succession to the late Dr. Stebbing, and Dr. Alistair Reginald French as the new secretary in succession to Dr. R. W. Durand. Sir Ernest Rock Carling and Mr. W. M. Mollison were re-elected president and treasurer respectively, and all the vice-presidents and retiring members of council were re-elected. An extraordinary general meeting was then held for the purpose of passing certain special resolutions, one of which authorized the Society to cover visitors from abroad who came to work in British hospitals, whether professors on exchange duty or practitioners coming over for postgraduate study.

MEDICAL DEFENCE UNION

The annual general meeting of the Medical Defence Union was held at its offices, 49, Bedford Square, W.C.1, on Sept. 28, with the president, Mr. St. J. D. Buxton, in the chair. Mr. Buxton said that the Union had been trying to help its members in matters resulting from the National Health Service Act, particularly with regard to partnership agreements, compensation, and superannuation. A memorandum had been prepared on points arising under Sections 35 and 36 of the Act (prohibition of sale of practices and compensation). Another piece of work concerned the question of consent to operation, on which several members had requested information. The council had sought opinion from a leading counsel and had embodied his views in a memorandum available to members on request.

Provision had been made during the year, Mr. Buxton continued, to overcome a difficulty which had caused the council much concern in the past. The council was now vested with full discretion in dealing with problems reported by members which affected the profession as a whole as well as the individual applicant. During the year the Union had dealt altogether with nearly 1,600 cases, 200 more than the previous year. The number of cases passed to the solicitors for attention was 117.

On the financial side the chairman said that already this year they had committed themselves to a sum in excess of £40,000 for indemnity and law expenses, and there remained more cases to be settled or fought in the courts. The highest figure until the year under review was in 1939, when these expenses were over £21,000. The subscription rate of £1 had not been changed, but at the meeting next year they might learn that the council considered it advisable to raise the subscription rate.

He concluded by expressing the indebtedness of the membership to Dr. Robert Forbes and Dr. P. H. Addison, the secretary and assistant secretary, and Mr. Oswald Hempson, the solicitor. The treasurer (Dr. Henry Robinson) drew attention to the fact that this year there was an excess of expenditure over income amounting to £1,340. The days when members could be charged a subscription of £1 and the Union show a handsome surplus at the end of the year were over, probably for ever.

Dr. J. C. Matthews, Dr. Henry Robinson, and Mr. A. Hedley Whyte, the retiring members, were re-elected to the council. The annual report, which was adopted at the meeting, dealt more extensively with the several matters touched upon by the president in his address.

WEST LONDON REMINISCENCES

Dr. W. S. C. Copeman, who took office as president of the West London Medico-Chirurgical Society on Oct. 22, devoted his address from the chair to the story of the West London Hospital and of the Society itself from their beginnings, the one in 1856 and the other in 1882, down to 1923, leaving the last quarter of a century to a later historian. Many famous names came into the narrative—Henry Maudsley, Alfred Cooper (father of Sir A. Duff Cooper, until lately ambassador at Paris), David Ferrier, Lenthal Cheatle, Charles Ballance, Stephen Paget, and, among early members of the Society, John Bland-Sutton, William Bennett, Jonathan Hutchinson, Howard Marsh, William Jenner, Samuel West. In 1859 Mr. Ernest Hart, later editor of the *British Medical Journal*, and at that time a popular contributor to *Household Words*, was elected to the staff of the West London. In the following year Sir William Crookes, the discoverer of thallium, was appointed analytical chemist to the hospital. The annual report of 1862 stated that the total number of patients seen at the hospital was 4,000, of whom 3,000 were "cured."

A member of the staff, Sir William Priestley, a descendant of the famous Joseph Priestley, was appointed physician-accoucheur to the household of Queen Victoria, and attained additional fame by sending in a bill for his attendance. The bill was paid, but Dr. Copeman thought his court appointment lapsed subsequently. The first reference in the hospital reports to the nursing staff was in 1882, when seven nurses were employed, but by 1898 there were 42 nurses. Those in training received no salary during the first year, £15 during the second, and £20 during the third, and any time off (including sick absence) outside the annual holiday of two weeks (three for sisters) had to be made up before they could matriculate.

The Society, formed as a result of a meeting of medical men convened at the hospital, took a high ethical line from the beginning. In its first year it expelled a member who had put "advice gratis" on his plate. The Society was caught on a wave of bacteriological enthusiasm in the late 'eighties, when, following an address by Mr. (later Sir Charles) Ballance, it was put on record that "probably within measurable distance of time each medical school will possess its own bacteriological laboratory, and this subject will be included in the curriculum." At the next meeting attention was drawn to the unsatisfactory nature of the operating theatre at the hospital, where out of 69 cases in the hands of one surgeon 11 had died of sepsis or gangrene, although "we are all antisepticists at the West London now."

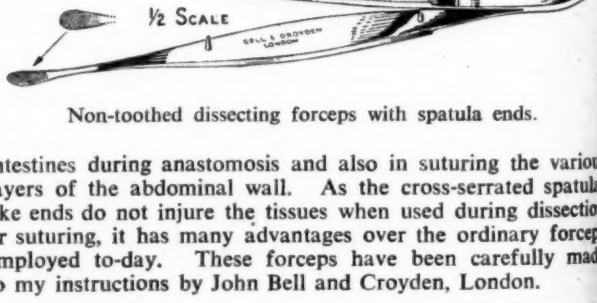
Meetings of the Society at about this period were notable for the length of the discussions. One result of this verbosity was that the editor of the *British Medical Journal* refused to print reports of the meetings for a couple of years until a deputation induced him to relent. Since that time, remarked Dr. Copeman, it had been the custom to invite the editor to the annual dinner. In 1900 a special meeting was called by the Society to discuss the possible use of motor-cars by medical men, but owing to the lack of interest nobody except the officers of the Society turned up. A better-attended meeting discussed at length the topical question of the best form of saddle for the safety bicycle.

In concluding his survey Dr. Copeman referred to the fact that in recent years a vigorous medical centre had grown up in the Society's area in the shape of the Postgraduate Medical School of London in association with Hammersmith Hospital. On this same evening the Dean of the School, Dr. C. E. Newman, and a number of distinguished representatives of the staff were admitted to membership of the Society.

Preparations and Appliances

NON-TOOTHED DISSECTING FORCEPS

Mr. RODNEY MAINGOT, surgeon to the Royal Free Hospital, writes: This non-toothed dissecting forceps is a modification of McIndoe's forceps, and is adapted from the pattern commonly in use in the United States. It is useful for holding



Non-toothed dissecting forceps with spatula ends.

intestines during anastomosis and also in suturing the various layers of the abdominal wall. As the cross-serrated spatula-like ends do not injure the tissues when used during dissection or suturing, it has many advantages over the ordinary forceps employed to-day. These forceps have been carefully made to my instructions by John Bell and Croyden, London.

The Chelsea Clinical Society held its opening dinner meeting on Oct. 12 at the South Kensington Hotel, with the president, Mr. Nils Eckhoff, in the chair. Dr. Geoffrey Evans read a paper on "Empiricism in Medicine" before 75 members and guests. Dr. Sundell, Mr. Geoffrey Parker, Dr. Daynes, and Dr. Lankester took part in the discussion which followed.

Correspondence

H 11 in Malignant Disease

SIR,—On behalf of the Hosa Research Laboratories we ask you to publish the following reply to the report (Oct. 16, p. 701) of the committee appointed by the Medical Research Council. The terms of reference of the committee were "to examine the evidence upon which is based the claim that H 11 is of value in the treatment of cancer in human beings." That evidence has not been examined.

1. *The report of the committee is based on only 2.7% of the 4,700 (now 5,600) cases.*—These 139 cases out of nearly 5,000 are not random samples as stated in the report, since they were chosen from a selected group of 1,000 cases which had died or ceased treatment and which in turn were selected in alphabetical order. The Laboratories are advised by a qualified statistician that the findings are therefore statistically fallacious and give no true impression of the total cases upon which the claim is based.

2. *The cases quoted from this selected group are atypical.*—Brief case records of twelve typical cases showing H 11 inhibitory action are appended. These (and all other cases) have been treated and reported upon by doctors and hospitals independently of these Laboratories. All of these and many others were available to the committee but have been ignored.

3. *Advanced nature of the cases treated.*—The report avoids mention of the fact that all the cases treated with H 11 were advanced, inoperable, considered untreatable, and rejected as hopeless by the clinicians concerned.

4. *Results too frequent to be fortuitous.*—In such advanced cases the high frequency and great reduction in tumour size caused by H 11 reported in large numbers of cases ignored by the committee cannot possibly be attributed to reduction of inflammation. Whether or not necrosis as a mode of regression is responsible for disappearance of tumours treated with H 11 (for examples see appended cases) is of no material consequence to the matter under discussion.

5. *Relief of pain.*—The high proportion of cases—e.g., 65% as based on figures quoted by the committee—in which pain is relieved does provide evidence of the value of the treatment. This is indicated by the facts that (*a*) loss of pain frequently occurs in cases in which narcotics had previously been necessary; (*b*) relief of pain commonly effected by H 11 in advanced cancer cases is not produced in patients suffering pain due to other causes; (*c*) histological evidence at the Laboratories (ignored by the committee) indicates that the relief of pain is due to inhibition of peripheral tumour growth.

6. *The experimental work is outside the terms of reference of the committee.*—On Feb. 19, 1945, the secretary of the committee wrote, "It is not within the terms of reference of the committee to examine the experimental evidence. Being accordingly concerned solely with clinical data . . ."

(*a*) *The experimental work which has been done on the Twort carcinoma is valueless.*—Table II shows that far more spontaneous regressions occurred in the controls than in the experimental animals! Incidentally, the figures in column 1 contradict the wording in column 4. Which is supposed to be correct? Properly selected, the control tumours at these Laboratories show a spontaneous regression incidence of less than 4%. The tumour forms a reliable one for investigation and the number of "takes" varies from 80 to 90%. It is interesting to note that another worker (Dr. E. C. Armstrong) in the Leeds Laboratory reported a 90% take with the Twort carcinoma and satisfactory growth during the period under review.

(*b*) *Failure to assess correct dosages.*—Since the investigators persistently refused to determine the correct dosage, work on the other tumours cannot be accepted. The Hosa Research Laboratories even offered to determine the dosages themselves if Dr. Bonser would send specimen tumours for grafting. The offer was ignored. There is no theory about the optimum dose of H 11; it is a fact. It may also be pointed out that variation in dosage does not depend upon volume changes but may relate to concentrations.

(*c*) *Failure to adhere to agreed conditions.*—The statement in the report that the conditions laid down were rigidly followed is not the case. For example, Dr. Bonser's figures submitted to the Laboratories show that the starting size of tumours varied from 4 × 4 mm. to as much as 10 × 13 mm. Such wide variation does not allow a reliable bio-assay to be performed. In spite of the fact that some tumours were many times the volume of this, all nevertheless were given the same dosage—and that a random dosage.

(*d*) *Misleading and erroneous statements in the report.*—Mention must be made of one in particular, that "Mr. Thompson, however, rejected five control and two experimental animals for reasons unstated." On March 25, 1947, Mr. Thompson wrote to the secretary of the committee fully explaining that these were rejected because fictitious figures had been given by the investigators to tumours which had not been measured. On June 30, 1947, every member of the committee was sent this information by the Laboratories. This statement should be retracted.

7. *Summary.*—We consider that in view of the complete inadequacy of the clinical investigations and the unreliability of the experimental work no serious investigation has been attempted. The Laboratories have received no intimation from the Medical Research Council that the process of examining the evidence had been terminated nor that publication was proposed. The Laboratories remained completely unaware of the report and its publication until the issue of the *British Medical Journal* containing it.

Abundant and incontrovertible evidence obtained from doctors and hospitals and open to qualified inspection exists at the Laboratories that H 11 can inhibit malignant growth in the human being.—We are, etc.,

J. H. THOMPSON.
G. J. W. OLLERENSHAW.

Sunbury-on-Thames, Middlesex.

CASE REPORTS

Case 1.—F., 56. Papillary cystadenocarcinoma (sectioned) R. ovary. First seen late 1944, visible and palpable tumour from 1 in. below umbilicus into pelvis. Radiographs suggested pressure on alimentary tract from without. Refused operation. 14/3/45, consented. Subtotal excision only possible owing to deep fixation to broad ligament. 4/45, deep *x*-ray 3 weeks. 8/45, abdominal swelling recurring, diagnosed recurrence and "untreatable." Prognosis under six months. 6/9/45, commenced H 11: weight under 8 st., falling; severe hypogastric and R.I.F. pain; some ascites; increasing abdominal mass as above. 23/11/45, no pain for two months; weight 8 st. 2 lb.; abdominal mass doughy; no ascites now. 10/4/46, weight 8½ st.; no pain; abdomen i.s.q., general condition good; housework. 23/3/47, examined under anaesthetic by surgeon who originally operated: no evidence whatsoever of carcinoma or obstruction or other abnormality; ceased treatment. 9/48, condition normal in all respects. Survival from commencing H 11: over 3 years.

Case 2.—F., 51. Carcinoma (sectioned) of ovary, excised 10/6/41, leaving clearly defined peritoneal metastases *in situ*. Massive ascites, recurred post-operatively, with 6 paracenteses (average 3 gallons) before starting H 11 on 1/7/41. 9/41, ascites absent since 8/41; general condition improved, gaining weight. 4/42, ceased treatment; general condition normal; no ascites (no paracentesis since H 11); N.A.D. abdomen or pelvis. Current report: normal health, sign- and symptom-free. Survival from commencing H 11: over 7 years.

Case 3.—F., 47. Carcinoma descending colon, first symptoms mid-1945. 19/10/45, laparotomy, inoperable primary, metastases in omental glands, left ovary. 31/10/45, commenced H 11: primary palpable 2½ × 1½ in.; some ascites; occasional blood and mucus p.r. 17/9/46, steady general improvement; *nil* abnormal now found clinically. 4/11/46, ceased treatment. 8/48, normal all respects. Survival from commencing H 11: 3 years.

Case 4.—M., 64. Osteosarcoma (sectioned) head of R. tibia. Paget's disease present many years; sarcoma developed 11/44, confirmed by *x*-ray 12/44. 6/45, onset increasing cough. 7/9/45, chest radiograph showed multiple secondaries upper and mid-zones both lungs. 8/10/45, commenced H 11; dyspnoea, increasing cough, occasional haemoptysis. 12/1/46, *x*-ray, some improvement, all opacities reduced, general condition static. Radiographs on 19/6/46, 8/11/46, 30/7/47, *et seq.*, indicate lung metastases static to date. No haemoptysis since 4/46. General condition static. Survival from commencing H 11: 3 years.

Case 5.—M., 43. Carcinoma (sectioned) of rectum, first diagnosed 2/46. 4/46, laparotomy and biopsy. Primary operable but liver metastases present, therefore colostomy only. 3/47, primary grown and now fills lumen of rectum, now considered inoperable. 11/3/47, commenced H 11; intermittent local pain; weight steady 8½ st.; primary as above, growing; liver not palpable. 4/47, gained 3 lb. weight; primary slightly softer, more mobile, lumen larger, liver i.s.q. 12/12/47, seen by surgeon: primary now freely mobile and considered operable. 29/1/48, complete abdomino-perineal excision of primary with ease; all observed malignant tissue removed; no evidence now of the liver metastases noted at first operation. Section:

adenocarcinoma, but showing "central necrosis attributed to H 11." 5/48, wound healed, sign- and symptom-free. 9/48, ditto. Survival from commencing H 11: 19 months.

Case 6.—F., 45. Epidermoid carcinoma (sectioned) of cervix uteri. Onset of symptoms 3/44. Radium early 4/44 after biopsy. 3/46, readmitted for vaginal haemorrhage. Telangiectasis near ureteric orifice was only abnormality found. 25/6/46, examined under anaesthetic and by cystoscopy: telangiectasis still present, no other abnormality. 1/47, small mobile hard mass R. pelvis, "certainly a recurrence"; no further treatment possible. 26/6/47, commenced H 11; weight 7¼ st., falling; intermittent severe pain (morphine); pelvic recurrence as above, growing; purulent vaginal discharge. 14/10/47, weight 8 st. 10 lb.; no pain now (no morphine); recurrence not now palpable; hospital report "improvement spectacular." 29/2/48, ceased treatment. 7/48, normal health. Survival from commencing H 11: 16 months.

Case 7.—F., 67. Malignant melanoma (sectioned) skin of arm, excised 1/4/46. Local recurrence, with secondaries on leg and face, early 1947. Radium 1/4/47 without response. 30/9/47, commenced H 11; weight steady 9 st.; no pain; all lesions growing. 24/11/47, all lesions much smaller, smaller ones having disappeared. 20/1/48, no lesions found. 29/2/48, ceased treatment. 6/48, normal all respects. Survival from commencing H 11: 13 months.

Case 8.—F., 50. Carcinoma of cervix uteri. Onset of symptoms 2/47. 4/47, deep *x*-ray. 19/6/47, commenced H 11; radiotherapist reported parametrium too much involved for deep *x*-ray or radium, inoperable. Weight 9 st.; mild pelvic pain, primary spreading. 16/10/47, weight steady; no pain now; up. 24/1/48, radiotherapist reported, "There has been quite a striking improvement in the state of the pelvis, presumably due to H 11. Feels better and pain not such a problem." 13/7/48, weight over 11½ st.; no symptoms; radiotherapist reported, "Vault of vagina and cervix clear of malignancy, possible suspicious induration L. uterosacral ligament; I see no reason for interference with the H 11 therapy." 1/10/48, gynaecologist reported cervix normal, less parametrial infiltration. Treatment continues. Survival from commencing H 11: 16 months.

Case 9.—F., 54. Carcinoma (sectioned) cervix uteri. Onset blood-stained discharge 9/44. First reported 5/47, diagnosis prolapse 7/47, admitted, carcinoma diagnosed (biopsy), inoperable. 26/8/47, radium for one hour only. Discharged 4/9/47, no further treatment possible. 20/9/47, commenced H 11; weight 9 st. 2 lb., falling; no pain; general condition fair; primary easily palpable, growing. 24/1/48, weight 10 st.; general condition better; vaginal examination primary considerably smaller. 11/5/48, gained 1 lb. weight; no symptoms; primary half its September size; no evidence of metastases. 11/6/48, seen at hospital; no trace of carcinoma. 26/7/48, ceased treatment. 15/9/48, i.s.q. Survival from commencing H 11: 13 months.

Case 10.—F., 41. Carcinoma (sectioned) L. ovary. Admitted 2/44, pelvic swelling. 12/2/44, laparotomy; malignant mass L. lower pelvis involving L. ovary and colon, inoperable; biopsy. 23/11/44, commenced H 11; moderate lumbar and rectal pain; hard mass filling pelvis but not palpable abdominally; glands palpable to L. of sacrum; growth apparently stationary since 2/44. 21/4/45, no pain now; p.v. scarring; abdominally i.s.q. 9/6/45, weight steady; no pain; few small hard masses in L.I.F.: scarring round cervix and corpus uteri, but now some mobility; slowly commenced cessation of treatment. 27/4/48, alive, well, symptom-free; abdominal condition static; masses now very small, hard, resembling fibrous (scar) nodules. Survival from commencing H 11: almost 4 years.

Case 11.—F., 62. Carcinoma L. lower bronchus. 7/5/43, chest radiograph L. lung field increased opacity from above downwards, corresponding with lower lobe, greater towards heart, indicates mass in lung; bronchus constricted at one point; diagnosis as above. 27/4/44, commenced H 11; primary radiologically stationary. No previous treatment. 25/8/44, condition static but gained 2 lb. weight. 1/45, *x*-ray film, lung mass completely liquefied; ceased treatment. 4/45, all fluid absorbed. 1/47, sign- and symptom-free since last report. 4/48, i.s.q. Survival from commencing H 11: 4½ years.

Case 12.—Transitional-celled carcinoma (sectioned) of bladder. 2/41–5/41, diathermy and deep *x*-ray to primary with good result. 9/41, secondaries in cervical and lumbar spine, deep *x*-ray 9/41–11/41, when liver first enlarged; no further treatment contemplated. 1/42, commenced H 11: weight under 7 st.; bed-ridden; jaundiced; severe spinal pain; liver grossly enlarged with palpable nodules. 15/3/42, weight 7½ st.; no pain now; walking steadily, some work; liver palpable but now no nodules; jaundice cleared. 5/5/42, weight 8 st. 2 lb.; no pain; walking out; liver smaller and much softer. 1/7/42, ceased treatment. 8/42, cystoscopy: bladder normal. Radiograph: entirely good. 10/42, back at full-time work. 1/43, radiograph: bony changes in spine stationary and sound; symptom-free. 25/6/45, weight over 10 st.; sign- and symptom-free; radiograph showed spinal lesions now completely re-ossified. Reports subsequently to date indicate normal health, sign- and symptom-free. Radiotherapist commented no similar result obtained by radiotherapy alone. Case published *B.M.J.*, Aug. 14, 1943 (p. 211). Survival from commencing H 11: over 6½ years.

SIR,—I have read with much interest the report (Oct. 16, p. 701) of the Medical Research Council's committee on this mysterious substance H 11. The conclusions of the report are clearly overwhelming; yet I would venture to make one criticism: there has been no controlled clinical trial of the substance.

The Hosa reports published are obviously valueless from the point of view of assessing the effects of H 11. Nevertheless, they would appear equally valueless in proving any lack of effect from H 11. Although the animal experiments are conclusive in themselves they are not necessarily an exact parallel to the condition in man. To quote but one example: stilboestrol is an accepted treatment for human prostatic carcinoma, and yet oestrogens are powerful carcinogens to experimental animals. I would hasten to add that, personally, I have no faith in H 11.—I am, etc.,

Twickenham, Middlesex. DAVID WHEATLEY.

SIR,—In your leading article on the above subject (Oct. 16, p. 716) you say that many organic substances have been employed as growth controllers and that "all have much the same effect. There is a transient diminution of pain, improvement in appetite and sense of well-being, and in many cases a diminution of the size of the tumour, often with softening at the margin or throughout. Very rapidly, however, the malignant process resumes its downhill course."

It is the claim of the Hosa Laboratories as I see it that one such substance, named for convenience H 11, has been investigated in much more detail than has ever been done before, and that in a few cases the inhibitory action has been so far intensified that incurable growths have actually disappeared and the malignant process has not resumed its downhill course. This is more than Mr. Thompson would ever claim, but I have before me three case reports which appear to prove that such a claim can be made good. Even if there should be only these three cases in three thousand there would still be a case for inquiry, for this proportion far exceeds that claimed by anyone for spontaneous regression in human beings, a condition much talked about—but has any medical man in this country ever seen a case of cancer, histologically proved, which recovered after all treatment had been given up as hopeless?

I admit, of course, that Mr. Thompson's results lack controls and stand up badly to statistical methods elaborated for the analysis of quite different material. He has inevitably been most severely handicapped by the fact that he is not a medical man, and by the further facts that the treatment is long, uncomfortable for the patient, and unsuitable for administration in hospital. How could he obtain controls or meet a demand for scientific recording beyond the scope of the general practitioner? He has moreover felt obliged to confine H 11 treatment to those adjudged to be hopeless cases, beyond the reach of surgery or any radiation. Nor has he had any opportunity for testing different dosages on human beings. In spite of all these very heavy handicaps he has produced such results as those now before me, and, for all I know, has others similar. These cases do not appear among those published in your last issue. They were presumably missed by the random sampling procedure favoured by the committee of the Medical Research Council. Nevertheless, that committee states, "Enough information is now available on which to form an opinion, and further work on the records is not advised," and your editorial announces a verdict of tried and found wanting.

I would suggest that Mr. Thompson has been ill-advised to rest his very moderate case (he claims no more than a significant inhibitory action) upon the slippery basis of animal experiments with the Twort cancer and unselected case records which were bound to be unsatisfactory by accepted standards. But I would suggest that your leading article and the committee's reports (p. 701) are equally at fault. Here in my hand are three case reports of hopeless cancer restored to health after treatment with H 11. These cases were among the Hosa records. Did the committee miss them? If it did, how can its opinion that no further record work is advisable be accepted? If it did not, if it actually considered these cases, why did it suppress any mention of such striking results? *Quis custodiet ipsos custodes?*

I do not wish to close this letter on a tendentious note nor to involve anyone connected with the Hosa Laboratories in my

personal views. I have had no communication with Mr. Thompson for over a year, but I am expecting to see him this week. I therefore send this letter to you before I can possibly be influenced by his opinions upon the report. In conclusion, I would suggest that a purely clinical committee should now investigate the Hosa records, not in order to produce a statistical summary but to report whether or not these records contain any evidence which warrants the continued use of H 11 and, if so, what further steps ought to be taken.—I am, etc.,

Sevenoaks, Kent. GORDON WARD.

Bronchial Asthma and Thiopentone

SIR,—I beg the opportunity of reporting the following case in the hope that it may serve as a warning against the administration of thiopentone to patients suffering from bronchial asthma.

A woman, aged 49, was admitted to hospital with carcinoma of the breast; she gave a history of "bronchitis and asthma" for the last sixteen years. General examination showed no abnormality of the cardiovascular system, and examination of the chest revealed increase in the respiratory phase on auscultation and rather high-pitched rhonchi over both lungs.

On the morning of operation she was given atropin. sulph. gr. 1/100 (0.65 mg.) at 9.40, and anaesthesia was induced with thiopentone (10 ml. of 5% solution) at 10.15, to be followed by nitrous oxide, oxygen, and "trilene." The patient became cyanosed as soon as the thiopentone had been given, and in spite of vigorous movement of the diaphragm and of the thoracic cage it was obvious that no air was entering the lungs. Laryngoscopy revealed a perfectly patent larynx, and the diagnosis of acute bronchial spasm was made.

By this time a little respiration had begun to take place, but the patient was still deeply cyanosed. A little ether was added to the oxygen, which had been flowing throughout, and an injection of 5 minims (0.3 ml.) of 1 in 1,000 adrenaline hydrochloride was given intramuscularly. At once the spasm became less marked, but it was at least half an hour before normal respiration took place.

I feel that the danger of administering thiopentone to asthmatics is not widely enough recognized and hope that this letter may serve as a reminder of the dangers inherent in this procedure.—I am, etc.,

Leicester. BRIAN D. L. JOHNSON.

Heart Block in Young People

SIR,—In the *Journal* of Dec. 6, 1947 (p. 906), we published a paper on heart block in young people. We have since had a communication from a member of the medical faculty of the University of Naples. We regard his letter as one of considerable interest, for it demonstrates in a striking manner how little the functional capacity of the heart may be affected by complete heart block in the young individual. Our correspondent, Dr. E. B., writes as follows:

"I am now aged 33, married, with three lovely, healthy children. My physical condition is excellent. My parents told me that I always showed bradycardia even in the first year of my life (now my normal pulse frequency is about 40 per minute). I think therefore that my disease is congenital, albeit there is another possibility, since at the age of 4 I received an injection of diphtheritic toxin-antitoxin mixture from a physician who suspected an initial stage of diphtheria. The first correct electrocardiographic diagnosis was established by a well-known German cardiologist, Fahrenkamp, when I was 12 years old. At that time I was sent by my father for my vacation to Germany, a guest of family friends. My exceptional bradycardia had been incidentally noted by the chief of that family on the occasion of a walking tour, and it was he who took me to his friend Fahrenkamp.

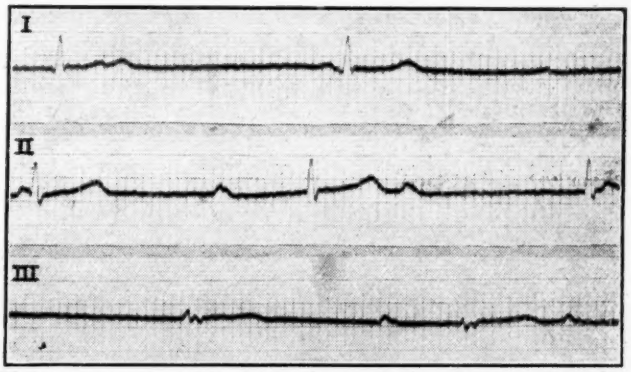
"Contrary to the advice of Fahrenkamp I have submitted my body to a great deal of physical stress. I have been a good tennis player, long-distance swimmer, alpinist (Mont Blanc, Monte Rosa, Matterhorn, Bernina, Piz Palu are amongst the mountains I climbed). During the last war I was a parachutist in the Allied Army and I directed a long mission in enemy-held territory; the physical and psychic stress was considerable, but I did not show any sign of cardiac trouble.

"Some years ago I had the opportunity of measuring the output of my heart under muscular work. I give some of the experimentally determined figures (unpublished) for the maximum stress (duration of the experiment 10 minutes): pulse frequency 98, breathing frequency 24.8, depth of breathing 2,412 ml.; pulmonary ventilation at standard conditions 48.9 litres per minute; oxygen consumption 2,967 ml. per minute; carbon dioxide elimination 2,976 ml. per minute; respiratory quotient 1.0; alveolar carbon dioxide pressure 46.38 mm. Hg; carbon dioxide virtual venous pressure 69.88 mm. Hg (technique according to Bock *et al.*—*J. Physiol.*, 1928, **66**, 121); blood minute volume 24.1 litres; systolic output 246 ml. (an extraordinarily high figure). The oxygen capacity of my blood is 20.3 (van Slyke's technique) and the red cell count is 5.2 million per c.mm.

"I can endure a long period of hard work much better than brief and violent exercise, but I never suffered faintness or any sign of heart insufficiency. Some hours after great effort I have sometimes noted fatigue and sleepiness together with a very pronounced bradycardia (about 35 per minute).

"I am 5 ft. 11 in. (1.8 m.) and weigh 12 stones (76.3 kg.). My parents and four brothers are in good health."

Our correspondent sends us a copy of an electrocardiogram taken by Professor P. M. Franco, Naples, which is reproduced here.



Electrocardiogram taken by Professor P. M. Franco, of Naples. The time-interval is 0.05 second.

This is yet another example of complete heart block, probably congenital, which over a period of more than 30 years has proved no hindrance in an unusually strenuous life.—I am, etc.,

Leeds. JOHN R. H. TOWERS, CONRAD BREMER.

Fibrositis

SIR,—Dr. James Cyriax (July 31, p. 251) has described simple facts which indicate that certain symptoms and signs cannot be explained by a lesion of muscle or muscle sheath but only by a lesion of a spinal joint. His critics attempt no alternative explanation of various aches and pains but boldly state that they are due to fibrositis—a disease which was postulated much less boldly by Gowers (*British Medical Journal*, 1904, **1**, 117), who himself stated, "We are without any direct evidence of the real nature of these affections, such as can only be furnished by the microscope." Would not the man who made this statement, if he were alive, now be the first to deny the existence of the condition he postulated?

If Dr. Cyriax's critics would produce microscopic sections of fibrositis their letters would be worth publishing. Without such sections they are not worthy of space in your journal. One critic complains that fibrositis has been interred with indecent haste. Surely after 44 years it is time that we buried a disease the existence of which was entirely supposititious and which has not been proved microscopically. Let us have no more of fibrositis. Let us have more scientific attempts to explain the many things that we do not know.—I am, etc.,

Mt. Hawthorn, Western Australia. JAMES H. YOUNG.

Sensitization to Sulphonamides

SIR,—In the very interesting leading article about sulphonamide combinations and sensitization (Sept. 18, p. 563) the author says: "It would be interesting if it could be shown *in vitro* that combination with protein is affected by sulphonamide concentration in the manner which these clinical findings would lead one to expect."

As far as I can see, it is just what I have shown in my paper "On Fixation of Sulfathiazole, Sulfapyridine, Sulfanilamide and Para-aminobenzoic Acid by Plasma" (*Acta Pharmacol. Kbh.*, 1945, **1**, 141).—I am etc.,

Copenhagen. A. HARRESTRUP ANDERSEN.

*** In the paper he refers to Dr. Andersen summarizes the results of his observations as follows: "By the addition of

plasma to solutions of the substances to be tested and ensuing ultrafiltration it is found that the curve for the fixation by the plasma is reminiscent of an adsorption curve, and the fixation is greatest for sulfathiazole, less for sulfapyridine, and least for sulfanilamide and para-aminobenzoic acid, in agreement with the ability of these substances to pass through the blood-liquor barrier."—ED., *B.M.J.*

Reactions to Intravenous Sclerotics

SIR,—I read Dr. C. E. Taylor's frank report (Oct. 23, p. 760) on his experiences with sodium morrhuate with interest. These facts speak for themselves regarding its dangerous constitutional effects. I have repeatedly emphasized these characteristics and believe that the use of this substance with its variable chemical composition should be abandoned.

Dr. Taylor now proceeds to praise sodium morrhuate: "I think I have used most of the intravenous sclerotics, but I have never found that any of them approach sodium morrhuate in reliability for giving satisfactory occlusion." I must point out that whilst it has bland local effects it has potential anaphylactic and lethal power in contrast to the rest of the sclerosant family, which, though they may cause injection ulcers, are seldom generally harmful.

Further, may I describe one of the newer sclerosants called P2G solution? It consists of phenol crystals 2%, glycerin 30%, and glucose 30% in apyrogen water. Mr. J. W. Riddoch, of Birmingham, introduced me to phenol 2% and glycerin 30%, but I did not find this so effective as the former, which has been used daily for over two years at consulting-room and out-patient injections (approximately 3,000, with doses of 3–5 ml.) and at operations (about 500, in volumes up to 45 ml.). It has been harmless in this series of patients. It is an effective local sclerosant, giving a good non-painful thrombosis that is only tender to the touch for a short time. It never incapacitates a patient from pain, as does "ethamolin" occasionally. When it is placed outside the vein an immediate sharp pain follows which makes the patient warn the operator to stop. This discomfort passes off within a minute by reason of the anaesthetizing action of the phenol. No injection ulcer has followed its use, although I have deliberately placed 2 ml. around a communicating vein in the hope of causing fibrosis around it as well as thrombosis inside.

At operation the usual dose is 5–10 ml. distributed down the internal saphenous vein to the knee and 5–7 ml. upwards from the ankle. A maximum of 45 ml. has been used several times. In a few instances the urine has been examined and a slight degree of carboluria found, but no harmful effect has been observed or reported. Occasionally after an injection a patient will report, if asked, a temporary giddiness, but it has always passed off within a few minutes and no one has ever required a stimulant or treatment for it.

P2G is made by most of the leading drug houses. I would beg Dr. Taylor to give it a trial and to finally lay aside that toxic and therefore dangerous fluid sodium morrhuate.—I am, etc.,

London, W.1. HAROLD DODD.

Femoral Hernia

SIR,—I must join issue with you over the slightly disparaging way in which you dismiss A. K. Henry's operation for femoral hernia. In your annotation (Oct. 23, p. 750) you state that Henry's operation "is useful for uncomplicated bilateral hernia in suitable patients, but in cases of strangulation the exposure may be inadequate." Since first reading Professor Henry's article I have used his approach routinely for all cases of femoral hernia, whether strangulated or not.

It has the following considerable advantages over both the low approach and the Lotheisen approach:

1. The inguinal canal is not interfered with and there is never any necessity to divide the inguinal ligament (Hey Groves).
2. Using a midline, paramedian, or Pfannenstiel incision the access to the femoral canal is much the same and with adequate muscular relaxation is good. If anything I prefer the Pfannenstiel—making the transverse incision rather more to the side of the hernia. The access is better, by way of comparison, than the access to the prostate by the retropubic method.
3. The operation takes much less time than either of the other two methods. Using the midline approach the scalpel has only to be lifted twice before coming down on the neck of the sac—once for the skin incision and again for the linea alba. Retraction of the peritoneum then brings the neck of the sac into view.
4. It is a simple matter to open the peritoneum in cases of strangulated hernia, and, having adequately isolated and cleaned the neck of the sac, I do this routinely in such cases; and thus one has complete control over the bowel when it is delivered from the sac.
5. The neck of the sac, which is the usual constricting agent, is dilated gently by the finger from the peritoneal aspect to allow delivery of the contents or may be divided by scissors with a finger protecting the bowel.
6. The pectineal fascia is used for closure of the canal after removal of the sac. This structure, which is an astonishingly stout one, is cut with a fine-bladed scalpel in such a way as to make a flap hinged either inferiorly or superiorly. The free edge is then sutured to the inguinal ligament.

It is a pity that this excellent approach, devised first by Lenthal Cheatle and later independently by A. K. Henry, appears to be so little practised.—I am, etc.,

Barry, Glam. H. M. GRANT.

Breast-feeding

SIR,—I was interested to read the article by Dr. Enid L. Hughes on "Breast-feeding in a Mining Town" (Sept. 25, p. 597), and was surprised at the low incidence of breast-feeding in Newbiggin—viz., 29% at three months. Prior to reading this paper the health visitors at one of the infant-welfare clinics in Southend had been keeping a record at my request of the mothers who were successfully breast-feeding at three months, with a view to ascertaining if any appreciable difference existed between women who were delivered in hospital and at home.

The numbers collected so far are small, 131 consecutive cases, of whom 89 were hospital deliveries and 42 home deliveries. Of the mothers delivered in hospital, including a large proportion of primiparae, 58% were fully breast-feeding at three months, and of the home deliveries 55% at three months. This difference may not be statistically significant, but it certainly does not bear out the view so commonly advanced that women delivered in their own homes are more likely to have a successful lactation than those confined in hospital. It is certainly encouraging to the staff of the Rochford General Hospital, where recently much greater latitude is allowed to the mothers in having their babies in cots by the bed and in being allowed to feed them at night and occasionally "off the clock."

In addition to these infant-welfare clinic cases I recently went through the records of 305 women attending the post-natal clinic in Southend six weeks after delivery. At the first attendance at this clinic all patients are asked whether or not they are breast-feeding, and the breasts are examined. If the child is wholly or partially bottle-fed the reason for weaning is noted. Of the 305 mothers 181 were wholly breast-feeding (59%), 100 mothers bottle-feeding (33%), and the remaining 8% were partially breast-feeding. Included in the 100 failures were seven cases where lactation was absolutely excluded—i.e., 4 stillbirths, 1 neonatal death, 1 pulmonary tuberculosis, and 1 congestive heart failure. There were six cases of primary failure in lactation, the babies being discharged from hospital wholly or partially on the bottle. In a further six cases lactation was abandoned because of local difficulties—cracked, flat, or retracted nipples, mastitis, and mammary abscess. In two-thirds of the remaining cases the reason for weaning was insufficiency of the milk supply—the milk "went," or the child was unsatisfied and failed to gain weight.

There remained still a substantial fraction of cases where breast-feeding was abandoned because of an excessive milk supply or because the child was ill. The history given was usually, "There was plenty of milk, but it didn't suit"; "The milk turned to water"; "The child vomited after feeds" (or had colic, diarrhoea, or sore buttocks). Hence the baby was often weaned, although gaining weight and thriving, and very often on medical advice. Two striking examples of such advice were a baby who developed pyloric stenosis, promptly weaned without investigation, and a premature baby, 5 lb. at birth, successfully breast-fed for 12 weeks when 8 lb. in weight, who was weaned on the family doctor's advice because it had vomited on one or two occasions.

My reason for writing at such length is mainly to suggest that general practitioners should consider carefully each case of difficult lactation brought to them, bearing in mind three questions: Is the baby underfed? Is the baby overfed? Is the baby sick? If the answer to the first question is in the affirmative then the appropriate treatment is to stimulate the breasts by changing from four- to three-hourly feeding, advising a night feed where necessary and a complementary, never a supplementary, feed in the early weeks of lactation; this rests and allays the apprehension of the harassed mother. If the child is ill or overfed it is bad logic and bad medicine to advise weaning. Finally, I would like to suggest that if the

family doctor has insufficient time to answer these questions himself he should refer the mother to those who have more time or experience—i.e., the local child-welfare clinic or the paediatrician of the area—before depriving the baby of its surest hold on health.—I am, etc.,

Westcliff-on-Sea, Essex. FLORA BRIDGE.

A Jelly-fish Sting

SIR,—While diving recently I was stung on the lower lip by a jelly-fish. The pain was rather like that caused by a severe sting from a nettle (*Urtica urens*), and within ten minutes there was a diffuse erythema measuring about 6 by 4 cm. running from the edge of the lip towards the point of the chin, with a white centre portion. An application of adrenaline 1:1,000 for some time failed to prevent an urticarial reaction, and the lip swelled, more marked in the mouth. The pain gradually became severe, the side of the face felt numb and unreal, like a Bell's palsy, and there was a considerable feeling of general irritability and malaise.

During the five days that followed the pain slowly decreased, but at the site of the sting a vesicular dermatitis developed, like an impetiginous infection, with a free serous discharge. The application of both chloroform and absolute alcohol appeared to have no effect, and the scar remained for a full fortnight. A fellow bather was stung at the same time and developed many large urticarial weals on the shoulders and buttocks.

Four days after the original sting and while the area was still discharging and painful I was stung again in three places around the left eye, between the brow and the lid, on the upper lid, and on the bridge of the nose in the area of the inner canthus. The pain commenced in the same manner, and within an hour a similar picture had developed—a large swollen area of erythema with a white centre. Tincture of *Urtica urens* was applied on damp cotton-wool and the pain rapidly decreased. Next day there was a slight sensation of soreness, but on the third day there was neither discomfort nor mark. The effects of this sting had completely disappeared while the first one was still in the course of recovery.

The local swimming-baths, which are tidal, frequently contain jelly-fish. At the end of this season the only ones which could be found were less than 2 cm. long (when afloat) and about 8 mm. in diameter, with a pale mauve central colouring. It is interesting, and most uncomfortable, to observe that such innocent-looking objects can cause a considerable local reaction and general malaise on what must be a very fleeting contact.—I am, etc.,

Guernsey. FRANK R. NEUBERT.

POINTS FROM LETTERS

Gastric Herpes Zoster

Dr. E. D. T. DONALDSON (Hale, Cheshire) writes: It may be of interest to your readers in view of the cases reported by Dr. R. V. Stone (May 8, p. 882) and by Dr. P. E. Fitzpatrick (June 19, p. 1206) to describe a further case of what I consider to be a true gastric herpes zoster. The patient, aged 65, had suffered from rheumatism of the right knee for some twelve months previously, for which she was in the habit of taking upwards of 15–20 gr. (1–1.3 g.) of aspirin daily. In August she complained of a severe pain in the right chest radiating round to the back. This was followed a few days later by a crop of lesions typical of herpes zoster affecting the 9th, 10th, and 11th thoracic segments. The pain was intense, and she complained a great deal of anorexia and nausea. One week later she vomited about a cupful of blood-stained material; this was not repeated although the anorexia and nausea continued. Her alimentary tract was *x*-rayed three weeks later—no abnormality being found. All symptoms have now cleared up apart from the original rheumatism. In this case the haematemesis may have been due to "erosion" as a result of taking aspirin, although I think its coincidence with the herpes zoster is too striking to be ignored.

Whooping-cough and Measles

Dr. FREDERICK ROTHENBURGH (Widnes, Lancs) writes: Referring to Dr. B. L. Hodge's (Aug. 7, p. 312) and Dr. S. N. Dhananjay's (Oct. 16, p. 725) letters, may I draw your attention to the fact that a sudden attack of pertussiform cough, with heavy fits similar to real whooping-cough, can be the first sign and the pre-stage of measles? This type of cough usually disappears when the measles rash appears.

Obituary

T. SHENNAN, M.D., F.R.C.S.Ed., LL.D.

Theodore Shennan, who died on Oct. 21, was professor of pathology at Aberdeen University from 1914 to 1936. Born at Bathgate, West Lothian, on March 9, 1869, he was the son of the Rev. Alex. Shennan. He was educated at the Royal High School and the University of Edinburgh, graduating M.B., C.M. in 1890 and proceeding M.D. in 1895. He obtained the F.R.C.S.Ed. in 1898. Shennan had early discovered his true vocation, and as pathologist to Leith Hospital in 1896 he began the career which was to lead him by way of the Royal Edinburgh Hospital for Sick Children and the Edinburgh Royal Infirmary to the lectureship on morbid anatomy at the university. Then in 1914 he was appointed professor of pathology at Aberdeen, and there he served his science and his university with distinction until 1936.

The chair of pathology in Aberdeen had been founded by Sir Erasmus Wilson in 1882. The first occupant of the Aberdeen chair was the redoubtable D. J. Hamilton, who, by the vigour of his personality and the forcefulness of his didactic teaching, had cast a spell which lingers to this day. Hamilton was succeeded in 1908 by one of his own students, George Dean, already a well-known serologist, but his bright promise ended with his early death after some years of ill-health. Shennan's task was an arduous one at the beginning. The outbreak of the first world war retarded the immediate development of his department, and in the post-war years, with only one assistant, he had to teach upwards of 200 students. But he triumphed over these difficulties and established for himself an enviable reputation alike as a teacher and as an administrator. He was dean of the Faculty of Medicine from 1915 to 1919 and again from 1925 to 1927. As chairman of the house committee of Marischal College for most of his tenure of the chair, he was busy with multifarious duties affecting the whole fabric of university life. He proved himself an invaluable member of the Senatus, which marked its appreciation of his work by appointing him as one of its assessors on the University Court. His lively interest in the student body never flagged; he served for many years on the committee of management of the Union and did much to encourage social and athletic pursuits.

Shennan will be remembered for his work as a morbid anatomist. The first edition of his textbook on *Post Mortems and Morbid Anatomy* appeared in 1912, the second in 1927, and the third in 1935. They embody the personal experience of a keen and accurate observer and contain a great store of useful information for the more mature pathologist as well as for the students for whom they were designed. In his earlier days he made notable contributions to the pathology of tuberculosis, particularly in childhood. There followed numerous publications in the *Journal of Pathology and Bacteriology* and elsewhere, culminating in an important monograph on dissecting aneurysms which was published by the Medical Research Council in 1934. Shennan was one of the original members of the Pathological Society of Great Britain and Ireland, and a well-known figure at its meetings.—J. S. Y.

C. H. MILBURN, O.B.E., M.B., M.S.

Charles Henry Milburn, a former member of Council of the B.M.A., died on Oct. 27, at Harrogate, at the age of 88. Most of his long life was spent in his native county of Yorkshire.

His father was the Rev. J. C. Milburn, and he was born at Sheffield in 1860. While a student at the Durham College of Science he won the Tulloch scholarship in 1879, and followed this at the Newcastle-upon-Tyne Medical School with prizes and medals in anatomy and physiology, public health, and surgery. He took the M.B. and M.S. degrees of Durham University in 1882, and was house-surgeon for three years at the Durham County Hospital. Then came a long period of work at Hull, where he was surgeon, and later consulting surgeon, to the Victoria Hospital for Children and the Hull and Sculcoates Dispensary. In 1897 Milburn was president of the Hull Medical Society. He joined the British Medical Association in 1882, and served it both locally and centrally,

being president in 1901 of the East Riding and North Lincolnshire Branch, for fourteen years a member of Council, and vice-president of the Section of Navy, Army, and Ambulance at the Annual Meeting in 1913. He was a member of the committee which reshaped the constitution of the B.M.A. in 1900 and of many other standing and special committees.

Ambulance work claimed a good deal of Milburn's energy before the 1914–18 war. He was deputy commissioner for No. 6 District of the St. John Ambulance Brigade from 1898 to 1903, and afterwards held high rank in the East Yorkshire Volunteer Brigade. He was also lieut.-colonel (honorary colonel), 2nd Northumbrian Brigade, Royal Field Artillery (T.F.), and a member of the East Riding Territorial Association. He went to France in 1915 and worked at Rouen as surgeon to No. 2 British Red Cross Hospital, where he was popular both with his medical colleagues and with the many officers who passed through his hands as patients. After a short time as surgeon to the Wharncliffe Hospital, Sheffield, he served on hospital trains in France and Belgium with the rank of major, and returned to England towards the close of 1918 to take up the duties of deputy commissioner at the headquarters of the Ministry of National Service. In 1919 he was appointed commissioner of medical services, and deputy director, Yorkshire Region, Ministry of Pensions, and a year later joined the staff of the Ministry of Health as divisional medical officer for the North-East of England, a post he held till 1925. Milburn was awarded the Volunteer Decoration, and for his services in the last war the O.B.E. He had many interests outside medicine. He was vice-president of the Kipling Society, and compiled for its journal a collection of epitaphs by Rudyard Kipling. He was also a justice of the peace and Deputy Lieutenant for East Yorkshire.

A kind-hearted unassuming man, Milburn went through life placidly doing whatever work came to hand. He was faithful in friendship and loyal to all the many institutions he had served. Deafness rather clouded his latter days at Harrogate, but he never complained, and it was characteristic of him that he should occupy some of his enforced leisure by combing local newspapers in search of items of medical interest for the *B.M.J.*

SUSAN ISAACS, C.B.E., D.Sc.

Mr. Nathan Isaacs writes: My attention has been called to your very full and just obituary notice of my wife, the late Susan Isaacs (Oct. 23, p. 763). May I offer a correction on a small point of fact which is perhaps not without interest or importance? You state that "when Geoffrey Pyke in the nineteen-twenties set up the Malting House School in Cambridge, Susan Isaacs welcomed his invitation to join the staff." The "staff," when the school began, consisted, besides my wife, of an untrained young girl who had looked after Pyke's small boy and was kept on as general help. The fact was that Pyke had the idea of starting a small model school where the most liberal and advanced educational ideas available at the time could be brought to bear on the early education of a group of young children. He advertised the idea in an arresting form, and my wife became interested in the opportunity which thus seemed to be offered. Pyke was prepared to provide the finance necessary to set the school going on an adequate and unhampered scale and to allow scope for its further development. Everything in fact pointed to the chance of carrying out an important pioneering experiment in education under the most favourable conditions, and my wife was finally persuaded to undertake to translate Pyke's idea into an appropriate reality.

Accordingly it was she who set up the school, starting from virtually nothing and on the agreed condition that she was to have an entirely free hand and the sole educational responsibility. This was only possible, of course, because Pyke's educational aims and outlook were in fundamental harmony with hers, and indeed he took the liveliest interest in the working and progress of the school, to which he made various suggestive and valuable contributions of his own. However, so far from my wife "joining the staff" of the school, she was actually its educational founder and remained its principal, in charge of the qualified staff which was gradually collected, until she resigned at the end of 1927. As through her work the Malting House School has passed into educational history, I trust that you will deem this correction worth publishing.

Dr. EDMUND SPENCER HEMSTED died on Oct. 7 at Kintbury, Berks, at the age of 78, only about a month after the death of his wife. He was the second son of Dr. Henry Hemsted, of Whitchurch, Hants. The founder of the family was a Dutch refugee who escaped from Holland at the time of the persecution by the Duke of Alva in the sixteenth century. Nine consecutive generations of the family have included members of the medical profession. One of these married in 1746 a Miss Rustat, whose family founded the Rustat Scholarships at Jesus College, Cambridge. Of Hemsted's six brothers, three were medical men and two were dental surgeons. After study at St. Mary's Hospital, Hemsted qualified as M.R.C.S., L.R.C.P. in 1892, and in 1895 started practice at Kintbury, on the Kennet, a few miles upstream from the much larger town of Newbury. About the turn of the century there were two or three practitioners in Newbury of undoubted academic distinction who yet lacked the gift of inspiring hope and confidence in their patients. These qualities Hemsted had in abundance, and before many years had passed he was attending not only everyone in and around Kintbury, but a good many patients from Newbury. His practice increased so rapidly that he had to take partners to cope with it; at his death he was the head of a firm of four, and remained in regular hard work until the onset of his last illness in July of this year. Hemsted was for many years honorary surgeon to the Newbury Cottage Hospital. In 1914 he tried to join the R.A.M.C., but was rejected on medical grounds, so he applied himself to service in war hospitals at Barton Court, Benham Court, and Albion House. He was a good shot and rider, and a keen fisherman. He contributed a paper on leucocythaemia to this *Journal* as long ago as 1896. In 1906 he married Miss Ellen Mary Stawell Brown, a well-known Wimbledon lawn tennis player who narrowly missed winning a title there, and actually did win a badminton championship in 1901. Of their three children, one, Dr. Edmund Henry Hemsted, is a member of the profession.—H. R.

Medico-Legal

THE LONGEST GESTATION PERIOD

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A member of the armed Forces last cohabited with his wife on Aug. 28, 1944, before going overseas. She bore a child on Aug. 12, 1945, and he petitioned for adultery, with the length of the period of gestation as the chief ground. Suggestions were made that other evidence existed which might tend to prove adultery, but these were rejected by the court. Judge Topham, K.C., who was sitting as a commissioner of divorce, heard medical evidence that it was not impossible for the husband to be the father of the child, and dismissed his petition. This decision was supported by the Court of Appeal on the ground that none of the unusual features of the pregnancy was sufficient to impel the court to reject the medical evidence and infer that adultery had taken place.

This period of 349 days is, we believe, the longest ever held by an English court to be possible. It supersedes the record set up last year in *Wood* v. *Wood*[1] of 346 days, and is far in excess of most of the limits set in foreign legislation. Sydney Smith says that periods of gestation beyond 300 days are distinctly unusual and suspicious, but quotes Dr. G. F. Walker's mention[2] in this *Journal* of one child born after 315 days and the cases in which children born after periods of 323, 324, and 336 days, weighed 12.5, 14, and 16.5 lb. (5.7, 6.1, and 6.5 kg.), respectively.[3] It will be interesting to see where the courts stop; or rather, as they follow the medical evidence, where the medical witnesses stop.

1 1947 2 All E.R. 95.
2 *British Medical Journal*, 1939, **1**, 1155.
3 Ibid., 1921, **2**, 220.

The National Association of Certified Nursery Nurses states that the organization is open to all nursery nurses holding a recognized nursery certificate. Nursery assistants who have completed five years' nursery work as associate members, and nursery superintendents, matrons, teachers, wardens, etc., are eligible for honorary membership. The annual subscription for full membership is 5s. Particulars may be obtained from the honorary secretary, Miss Holmes, St. Anne's N.T.C., Binfield Park, Bracknell, Berks.

Medical Notes in Parliament

A new Session of Parliament was opened by the King on Oct. 26. The Speech from the Throne announced that legislation would be introduced changing the constitution of the General Nursing Council and to provide for the better training of nurses. Another Bill will provide for safer milk. Improvement of water supplies in Scotland and amendment of the Scottish criminal law are also proposed subjects for legislation.

Bills introduced on Oct. 27 included the Education (Scotland) Bill, which proposes among other things to amend the provisions of other Acts relating to defective children and the employment of children.

Replying to Sir IAN FRASER on Oct. 29 during the Debate and Address, Mr. HERBERT MORRISON said that in the opinion of the Government the case for a Select Committee to consider war pensions and allowances was not made out. He pointed out that since 1946 further improvements had been made.

Mr. SOMERVILLE HASTINGS spoke on the training of nurses and the legislation proposed on this point. He said the coming legislation for this purpose would succeed or fail according to whether it made possible the ultimate complete separation of the authority for training nurses from the authority for providing treatment for the sick. The constant conflict between the duty of the nurse to herself and her duty to her patients resulted in many nurses leaving the profession during training or as soon as they were trained. The employer could not successfully be the teacher, and the hospital authority which asked a matron to be both asked her to carry out an impossible task. The nurses' course need not be a long one. It could be carried out successfully in two years, but the student nurse must be a student like other students. Her life should be spent like theirs in hostel, home, or lodgings. Much could be done by arranging the curriculum of the nurse and the time she spent in the wards on the same lines as those of the medical student.

The debate was adjourned.

P.P.S. to Mr. Bevan.—The Minister of Health has appointed Mr. J. E. Beddoe to be his Principal Private Secretary.

Universities and Colleges

UNIVERSITY OF OXFORD

In a Congregation held on Oct. 14 the following medical degrees were conferred:

M.CHIR.—*E. G. Tuckwell.

M.B.—E. J. E. Jones, R. G. Chambers, Zaida M. Megrah, Mrs. Jean C. Toynbee, *H. A. Evans, *A. R. Wilson, *J. W. Platt, *A. C. Cox.

* In absence.

UNIVERSITY OF GLASGOW

A series of five lectures on "The History of Medicine," by Dr. Douglas Guthrie, began on Oct. 26. The second lecture was given on Nov. 2 and the remaining three will be delivered in the Zoology Lecture Theatre of the University on Nov. 9 and 30 and Dec. 7, at 4.30 p.m. They are open to members of the University, and to the public, without ticket. Details will be published in the diary column of the *Journal*.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on Oct. 28, with the president, Lord Moran, in the chair, Dr. J. H. Sheldon, Dr. J. M. H. Campbell, Dr. E. R. Cullinan, and Sir Weldon Dalrymple-Champneys were elected Councillors.

The following were elected representatives of the College: Dr. H. E. A. Boldero on the Committee of Management of the Conjoint Board; Dr. F. S. Langmead on the Central Midwives Board; the President, Sir Leonard Parsons, Dr. H. E. A. Boldero, Dr. W. G. Barnard, and Sir Allen Daley on the Standing Joint Committee of the three Royal Colleges; Dr. C. M. Hinds Howell, Dr. T. C. Hunt, Dr. J. C. Hawksley, and Dr. J. B. Harman on the Committee of Reference; Dr. C. M. Hinds Howell and Dr. J. B. Harman on the Central Medical War Committee; and Dr. Donald Hunter on the Poisons Board.

Sir Weldon Dalrymple-Champneys was appointed Milroy Lecturer for 1950, his subject being "Undulant Fever, a Neglected Problem."

The President announced that the Jenks Memorial Scholarship had been awarded to Martin Lawson Crossfill, late of Epsom College.

Membership

The following candidates, having satisfied the Censors' Board, were elected Members:

I. Anderson, M.B., M. W. Arthurton, M.B., H. S. Baar, M.D., D. W. Barritt, M.B., R. E. Beamish, M.D., A. C. Blandy, M.B., H. J. Boutourline-Young, M.D., R. J. K. Brown, M.B., J. A. Campbell, M.B., C. O. Carter, B.M., F. B. E. Charatan, M.B., J. A. H. Collyns, M.B., E. G. Cook, M.B., R. I. G. Coupland, M.B., R. H. Cutforth, M.B., D. F. Davies, M.B., D. M. Davies, M.D., P. D. B. Davies, M.B., W. Dickson, M.B., A. Dolphin, M.D., B. V. Earle, M.B., J. R. D. Eaton, M.B., A. El-S. Eissa, M.B., H. L. Ellis, M.D., C. C. Ewart, M.B., A. N. Exton-Smith, M.B., W. Fabisch, M.D., D. A. Ferguson, M.D., H. V. L. Finlay, M.B., P. B. Fox, M.B., T. T. Fulton, M.D., I. Gilbert, M.B., S. V. S. Govinda Setty, M.B., M. J. Greenberg, M.B., C. Gresson, M.B., J. R. Harries, M.B., R. V. Johnston, M.B., E. C. B. S. Keat, M.B., J. O. Laws, M.B., A. G. Leishman, M.B., I. C. Lewis, M.B., G. H. T. Lloyd, M.B., Josephine M. Lord, M.B., L. C. Lum, M.B., R. H. G. Lyne-Pirkis, M.B., A. R. Lyons, M.D., R. K. MacCuish, M.B., A. C. Macdonald, M.B., G. Macdonald, M.D., L. E. McGee, M.B., J. K. Martin, M.B., H. Miller, M.B., I. Miller, M.D., E. H. Minors, M.B., B. S. Moos, M.D., A. A. Morgan, M.B., J. Nash, M.D., S. R. K. Padmavati, M.B., I. C. L. Patch, M.B., S. H. Patel, M.B., M. B. Pemberton, M.B., A. R. Piracha, M.B., E. MacL. Poulton, B.M., F. I. Rackow, M.B., D. H. Reilly, M.D., P. K. Renshaw, M.B., P. L. Robinson, M.B., R. S. Savidge, M.B., J. Shein, M.B., G. Skinner, L.R.C.P., A. W. Sloan, M.B., W. H. Smith, M.D., W. G. Spector, M.B., M. P. Spence, M.B., J. W. Stephens, L.R.C.P., J. P. P. Stock, M.D., D. H. P. Streeten, M.B., J. L. Taylor, M.B., R. W. Temple, M.B., H. R. Thomson, M.B., P. A. Thorn, M.D., E. Waddington, M.B., D. C. Watson, M.B., S. P. B. Way, M.B., W. Whitaker, M.D., J. B. Wild, M.B., H. B. Ll. Williams, L.R.C.P., Iolo G. Williams, M.B., F. B. M. Woodhouse, M.B., D. G. Wraith, M.B., G. A. Wright, M.B.

Licences

Licences to practise were conferred upon the following 146 candidates (including 33 women) who had passed the Final Examination in Medicine, Surgery, and Midwifery of the Conjoint Board, and who have complied with the necessary laws:

M. S. M. Adams, Maureen B Adams, D. A. Ager, D. D. Alexander, H. D. Alexander, J. D. Arneaud, N. O. Ascroft, K. A. Baker, K. L. Batten, D. F. Bedford, D. P. Belgrave, S. Benaim, G. R. Benett, Elizabeth Bennett, J. M. Bernstein, A. I. Berwitz, T. B. Binns, J. A. L. Bonnell, P. H. Bracewell, A. T. Broadbridge, Ena K. Bruck, R. J. Carey, J. K. Carter, W. I. Carter, J. A. Cheese, Ellen M. Chippindale, M. Cohen, W. W. H. Colmer, Elizabeth D. Connan, W. E. Cooper, A. A. Craigen, Phyllis A. M. Crozier, D. A. Davey, D. H. Davies, G. J. Davies, Gwenhwyfar Davies, V. J. E. Davies, Nuala M. Dowdall, R. W. Doy, Shirley R. Drake, B. H. du Heaume, Gwenllian Edwards, A. A. Eley, Mary G. Ellis, H. B. F. Fairley, J. Fine, C. A. Foster, Lois Gardiner, R. Gardner, G. M. Gould, A. A. Graham, Edwina E. Green, H. J. A. Hahn, D. C. Hall, J. A. H. Hancock, D. F. N. Harrison, J. M. Haughton, G. E. Haward, R. B. Heisch, A. A. Hobbs, P. H. Holden, C. I. Hood, J. C. Humber, K. M. S. Hume, Marjorie J. Ion, T. E. Jeffreys, Beryl M. Joles, C. R. Jolly, D. H. Jones, Miriam Kahn, M. A. Kalina, A. J. Karlish, M. S. Kataria, H. R. Ker, E. Killey, G. S. Laing, P. Lancer, B. H. Lawrence, Gerda Lewin, E. A. C. Lloyd, V. A. Lloyd, Mary Lloyd-Evans, F. A. H. Logie, R. H. Longton, J. A. Ludwig, B. Lytton, Elizabeth G. S. McDowall, M. H. Masina, Leela Menon, J. Monckton, D. K. Morgan, D. McK. K. Muir, J. G. Neville, W. T. Newman, Anne Nunan, H. M. C. O'Driscoll, Jean M. Ottaway, K. Ll Owen, J. J. Owies, O. Parry-Jones, Jacqueline I. C. Payne, G. W. Pearce, M. C. Peterside, E. M. Poulton, D. G. Price, Margaret D. E. Quinet, B. W. Richards, D. F. Richards, J. L. Richards, W. R. Riley, I. R. L. Rose, Marian W. Ruscoe, D. G. Rushton, J. M. S. St. John, E. R. J. Sarfati, H. J. Sayani, W. K. Schnarr, D. N. M. Scott Warren, R. G. Seager Thomas, S. A. V. Serviss, Pauline M. Seymour-Cole, P. W. Shillito, D. W. Smith, R. S. Sneath, D. H. K. Soltau, Margaret Speight, G. D. Starte, G. A. Steele, Mildred A. R. Stilson, Mary C. Sumption, R. L. H. Tasker, D. G. Taylor, Margery W. Taylor, J. Tintner, D. A. T. Tizard, Jean M. Tomlinson, J. T. Trencham, S. E. Trickey, P. G. Tuffnell, R. J. Vale, J. S. Vazifdar, T. Wade-Evans, P. R. Wagner, Norma M. Whalley, F. R. H. Wrigley, J. R. W. Wynne.

Diplomas

Diplomas in Tropical Medicine and Hygiene, in Ophthalmic Medicine and Surgery, in Child Health, in Industrial Health, and in Physical Medicine were granted jointly with the Royal College of Surgeons of England to the following successful candidates:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—To the 30 successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England.

DIPLOMA IN OPHTHALMIC MEDICINE AND SURGERY.—To J. S. McKenty and to the 52 candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England.

DIPLOMA IN CHILD HEALTH.—To M. F. Moses and to the 87 candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England.

DIPLOMA IN INDUSTRIAL HEALTH.—To the 12 candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England.

DIPLOMA IN PHYSICAL MEDICINE.—G. H. Dobney, D. M. L. Doran, Joan M. Gold, G. Gregg, J. B. M. Milne, K. W. N. Palmer, J. D. Thompson, M. E. Wigfield, R. W. Windle.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

A meeting of the Board of Faculty of Anaesthetists was held on Oct. 6, with Mr. A. D. Marston, the Dean, in the chair. Some 19 newly elected Fellows of the Faculty were introduced by the Dean and admitted to the Fellowship of the Faculty by the President of the College, Lord Webb-Johnson.

It was decided that whereas up to the present only holders of the Diploma in Anaesthetics of the two Royal Colleges should be

eligible for Membership of the Faculty, in future, holders of the Diploma in Anaesthetics of other recognized bodies should be eligible for admission.

It was reported that there had been an excellent response to the first course of lectures and tutorials which had been organized by the Faculty. The Board is anxious to increase the scope of its teaching and is hoping to arrange for clinical instruction to be given at various non-teaching hospitals.

A Joseph Clover Memorial Lecture has been founded by the Faculty and is to be given annually. Mr. A. D. Marston was elected to give the first of these lectures at the College on March 16, 1949, after the annual general meeting of the Faculty.

The Dean presented to the Faculty a gold badge of office to be worn by Deans of the Faculty. The Board presented to the College, to commemorate the founding of the Faculty and the Fellowship, a silver claret cup, once the property of Professor Simpson and presented to him by Lord Errol, and a silver-gilt cup which is a replica of a cup designed by Paul Lamerie in the seventeenth century. The Board gave a small dinner-party in the College in the evening, to which a few guests were invited.

The following were elected Fellows of the Faculty: H. K. Ashworth, Wesley Bourne, S. F. Durrans, H. E. Karslake Eccles, A. H. Galley, Noel Gillespie, Victor Goldman, John Halton, A. E. W. Idris, R. W. Ironside, F. Barnett Mallinson, Mrs. H. Scott Mason, Mrs. K. L. Oldham, Mrs. E. M. Taylor, Ralph M. Waters, Keith Woodruff.

At a meeting of the Council held on Oct. 14, with the President, Lord Webb-Johnson, in the chair, Professor Geoffrey Hadfield was admitted as Sir William Collins Professor of Human and Comparative Pathology, and the John Tomes Prize was presented to Professor H. H. Stones, of Liverpool. The following were appointed Bland-Sutton Scholars: Mr. R. J. Last (reappointed) and Mrs. P. H. Herbert.

The Fellowship in Dental Surgery was awarded to Dr. Harvey H. Reid (Canada) and to Professor B. Gottlieb (Austria).

Diplomas of Membership were granted to R. B. Heisch, C. I. Hood, and D. H. K. Soltau.

Diplomas in Tropical Medicine and Hygiene, in Ophthalmic Medicine and Surgery, in Child Health, and in Industrial Health were granted jointly with the Royal College of Physicians of London to the following successful candidates:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—C. S. Agrawal, M. H. S. El Amroussi, Norah H. C. Clarke, B. P. Courtenay-Mayers, K. O. Courtney, R. McP. Cross, R. S. Dayal, H. G. Edmunds, W. Fabisch, J. D. Grene, J. T. Harold, G. F. Houston, M. H. Hughes, S. A. Jones, R. Lwin, G. McHugh, B. U. Mistry, Mok Hing Yiu, R. Panigrahi, M. Rech, A. S. Saffar, M. A. El Sayed, S. C. Sekar, A. K. Sen, F. K. Shah, W. D. L. Smith, M. L. Sur, E. Tustanowski, G. H. Wattley, Wu Hsueh-Tsung.

DIPLOMA IN OPHTHALMIC MEDICINE AND SURGERY.—R. C. Agarwal, A. N. Ashworth, N. L. Bailey, S. C. Banerji, G. M. Barling, B. A. Bembridge, T. A. S. Boyd, R. S. E. Brewerton, J. B. Bunting, T. Chadderton, R. M. Chambers, Shing-Chue Chan, P. M. Chaudhuri, E. S. Dismorr, N. F. Donaldson, S. Etzine, J. H. W. Fagan, P. I. Franks, S. Galbraith, P. J. A. Gormley, T. B. Gupta, Ko Gyi, A. Harrison, J. R. Hudson, P. J. L. Hunter, R. I. Jaffe, K. R. Kesavachar, T. G. Kletz, M. Lerner, H. F. T. MacFetridge, B. A. Marshall, T. S. Maw, M. Mohsin, L. Myers, W. J. Naunton, M. J. Nikosiewicz, Eithne J. O'Riordan, C. M. Phillips, S. T. Puttanna, J. E. Pyper, J. L. Reiss, K. Rubinstein, H. Saiduzzafar, A. E. Sawday, M. Shaffi, E. Shenken, N. I. Sreenivasan, C. S. Swan, J. Swartz, A. K. Tulloch, J. M. Whaites, P. C. Yates.

DIPLOMA IN CHILD HEALTH.—H. C. Allan, S. Balasingam, Marion B. Bethune, S. Bhattacharjee, Camilla B. P. Bosanquet, T. A. Brand, E. J. S. N. Briggs, F. B. Bromfield, H. J. S. Brown, Isobel McA. Brown, M. F. G. Buchanan, L. J. Bussell, Helen A. Cawson, A. B. Christie, Margaret T. Collins, W. D. D. Cooke, E. G. A. Crawshaw, J. U. Crichton, P. O. Crossfield, G. H. R. Curnock, W. Davies, A. W. Dickie, M. H. C. Dyson, P. D. Fergusson, R. J. L. Ferris, H. J. W. Fisher, I. H. Fletcher, J. O. Forfar, Frances A. Fouracres, Gin Shan-Yah, Janet F. Graham, J. R. Harries, Dorothy A. Harvey, K-ul W. Hazratji, Betty E. Howarth, M. C. Hudson Bennett, Pauline M. Jackson, J. C. Johnson, R. St. J. R. Johnston, G. Kirtane, Stephanie A. Laing, B. M. Laurance, J. A. Leitch, R. Lindop, R. H. G. Lyne-Pirkis, Kathleen J. McCarthy, Muriel M. McLean, H. B. Marsden, Margaret St. C. Masson, Gladys A. Meigh, Rachel Menashe, S. M. Merchant, H. R. A. Michelmore, Dorothy J. Miller, R. G. Mitchell, E. S. Monteiro, J. N. Montgomery, N. M. Nicholson, W. B. O'Driscoll, E. J. Parr, J. Pelunsky, A. P. Radford, Elizabeth Radovitch, J. T. Rendle-Short, G. A. V. Ribeiro, F. Riley, B. S. Rose, D. C. Ryan, M. Shah, Gwendolen D. Smith, P. Stevens, B. Strickland, P. V. Suckling, Jean C. Taylor, K. B. Thornton, Joyce F. Tucker, C. H. C. Upjohn, D. F. Van Zwanenberg, D. G. Vulliamy, G. F. Walker, J. M. Watt, L. E. Wear, S. D. V. Weller, R. W. Wilkinson, Jean C. Willison, B. S. B. Wood, L. A. Zeki.

DIPLOMA IN INDUSTRIAL HEALTH.—T. S. Adisubramaniam, M. A. C. Dowling, W. Gunn, M. N. Gupta, E. T. Harrison, G. O. Hughes, T. H. McCormack, L. E. J. Poulier, J. B. Sherman, J. A. Smiley, J. M. Stuart, A. R. Thompson.

The Bai Jerbai Wadia Hospital for Children was recognized in respect of the posts of surgical registrar and first and second house-surgeons for a period of six months, in connexion with paragraph 23 of the F.R.C.S. regulations.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Professor D. M. Dunlop will deliver the Finlayson Memorial Lecture in the Hall of the Royal Faculty of Physicians and Surgeons (242, St. Vincent Street, Glasgow) on Wednesday, Nov. 10, at 5 p.m. His subject is "The Clinical Use of the Antihistamine Drugs." Other lectures will be given in the Hall of the Faculty on Wednesdays, Nov. 24 and Dec. 8, 1948, and Jan. 12 and 26, and Feb. 9, 1949, at 5 p.m. Details will be published in the diary column of the *Journal*. Medical practitioners are invited to attend.

No. 42

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Oct. 16.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948					1947 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	36	5	10	—	1	44	4	24	1	1
Deaths		1	1				—	1		
Diphtheria	141	8	43	17	3	202	22	64	12	1
Deaths	1	—	—	—	—	2	—	—	—	—
Dysentery	114	9	70	—	1	46	4	47	1	—
Deaths					—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			23	11	2			24	7	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				51					101	
Deaths	22	1	4	4	3	60	2	20	10	5
Measles*	4,536	78	74	49	66	1,797	63	84	192	11
Deaths†			1	—	—	1	—	—	1	—
Ophthalmia neonatorum	55	6	7	—	—	67	5	10	—	—
Deaths										
Paratyphoid fever	9	4	4 (B)	—	—	16	—	2 (B)	1 (B)	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	479	25	1	3	—	531	35	4	2	2
Deaths (from influenza)‡	7	1	1	—	1	11	5	—	—	—
Pneumonia, primary			163	16				184	16	
Deaths	171	23		3	6		18		6	6
Polio-encephalitis, acute	7	1				12	1			
Deaths							—			
Poliomyelitis, acute	81	5	5	4	—	276	24	55	10	6
Deaths§	8	1					1			
Puerperal fever		—	9		—		—	18		—
Deaths										
Puerperal pyrexia‖	100	11	6	—	1	113	6	14	—	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,519	103	324	206	36	1,352	116	267	81	49
Deaths†			—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	12	1	2	1	—	7	—	4	3	—
Deaths	1	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,949	146	83	22	10	1,009	87	28	37	6
Deaths	4	—	1	—	—	2	—	—	1	—
Deaths (0–1 year)	258	27	33	19	6	335	40	74	27	9
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	4,336	718	562	139	118	4,023	610	546	184	84
Annual death rate (per 1,000 persons living)			11·3	8·7				11·4	11·6	
Live births	7,491	1220	929	338	237	7,981	1300	1045	355	239
Annual rate per 1,000 persons living			18·7	21·1				21·0	22·4	
Stillbirths	197	21	28			222	25	30		
Rate per 1,000 total births (including stillborn)			29					28		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Food-poisoning at Southgate

An outbreak of food-poisoning has been reported from Minchenden County Grammar School, Southgate, London, N.14. Approximately 500 pupils and staff partook of a midday meal served in the school canteen on Thursday, Oct. 21. About 150 of those who ate the meal—it has not yet been possible to ascertain the exact number—complained of diarrhoea and severe abdominal pains during the evening of the same day or at night. In a few instances nausea and vomiting were also present, with headache, although there was no evidence of pyrexia. The symptoms passed off rapidly, all the members of the staff and most of the children attending school on Friday, Oct. 22. By the following day few after-effects were reported.

The midday meal on Thursday consisted of salt beef, salad with salad-dressing, potatoes, and baked almond tart. Bacteriological examination of the beef, carried out by the Central Public Health Laboratory, showed evidence of fairly heavy bacterial growth. The method of cooking the beef, which had been stored in brine (concentration 16%), was as follows:

The meat was delivered to the canteen on the morning of Wednesday, Oct. 20. It was immediately placed in the refrigerator, in which it remained until the afternoon of the same day. It was then removed and cooked in a gas boiler for two and a half hours. After cooking, the meat was allowed to cool off in the boiler during the night of Oct. 20–21, being served cold, with salad, on the following day. It would appear that the cooling-off process provided conditions in which bacteria could multiply and elaborate toxins.

An interesting feature revealed by the investigation was that similar joints from the same batch of salt beef were supplied to two other school canteens in the area, and were cooked in the manner set out above. In these cases, however, the meat was not allowed to remain in the boiler to cool after cooking, but was removed, placed on covered trays, allowed to cool, and was then put in the refrigerator.

Bacteriological investigations are still continuing, and it has not yet been possible to identify the responsible organism. It might be stated in conclusion that conditions in the school canteen were very satisfactory and that the standard of hygiene there left nothing to be desired.

Discussion of Table

In *England and Wales* increases were recorded in the incidence of measles 475 scarlet fever 246, acute pneumonia 58, dysentery 30, and diphtheria 29, while a decrease was recorded in the notifications of whooping-cough 124.

The largest rises in the incidence of measles were in Yorkshire West Riding 151, Monmouthshire 99, Essex 91, and Yorkshire East Riding 77. In contrast to the general increase a fall occurred in the south midland counties, where the notifications declined from 148 to 90.

Notifications of scarlet fever have been doubled in the past six weeks since the incidence began to rise. During the week the largest increases were Lancashire 48, Essex 29, and London 28. For nine consecutive weeks a fall has been reported in the incidence of whooping-cough; the local variations in incidence were small.

The return for diphtheria was the largest for thirteen weeks. In Lancashire the notifications of diphtheria showed a rise of 14 due to an increase in the county boroughs. An outbreak of diphtheria affecting 6 persons was notified from Durham, Houghton-le-Spring U.D.

In Shropshire, Oswestry R.D., 6 further cases of typhoid fever were notified. An outbreak of dysentery affecting 50 persons was notified in Essex, Hornchurch U.D. The other large return of dysentery was 9 cases in Warwickshire, Warwick R.D. In Lancashire only 8 cases of dysentery were notified; this was 20 less than the figure for the preceding week. The largest returns of acute poliomyelitis were Lancashire 8, Middlesex 7, Northamptonshire 7 (Kettering M.B. 6), London 5, and Devonshire 5.

In *Scotland* an increase occurred in the number of notifications of scarlet fever 76 and whooping-cough 19 and a decrease was recorded for dysentery 18. The decreased incidence of dysentery was mainly due to a fall of 15 in the notifications from the western area. A rise in the notifications of scarlet fever was general throughout the country except in the north-eastern area, where a small decline occurred.

In *Eire* a decrease was recorded in the number of notifications of measles 36 and whooping-cough 26, while a rise of 32 was reported for scarlet fever. These trends applied to most areas of the country. A further 25 cases of measles were notified from the outbreak in Clare, Kilrush R.D. The largest returns for scarlet fever were Dublin C.B. 146 and Galway U.D. 12.

In *Northern Ireland* a decrease of 38 was reported in the number of notifications of measles from Belfast C.B.

Week Ending October 23

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,389, whooping-cough 2,163, diphtheria 153, measles 5,303, acute pneumonia 426, cerebrospinal fever 31, acute poliomyelitis 76, dysentery 99, paratyphoid 4, and typhoid 13.

Medical News

Medical and Biological Abstracting

To avoid duplication of effort among certain abstracting services, an Interim Co-ordinating Committee on Medical and Biological Abstracting was set up in October, 1947, by Unesco and will now be jointly sponsored by the World Health Organization. Arrangements have been made to exchange abstracts between some of the agencies concerned. The experiment is still in progress. The Interim Committee, believing that its work can be usefully continued, has invited certain other non-profit-making organizations in the field of medical and biological abstracting to serve on it. When these invitations have been accepted, a full meeting of the Committee, which will then cease to be interim, will be held in Paris in the summer of 1949. Any organizations interested in this work should communicate with the Department of Natural Sciences, Unesco, Unesco House, 19, Avenue Kléber, Paris XVIe.

Clergy's Appreciation of Medical Profession

The Lower House of Convocation of Canterbury recently passed the following resolution:

"That, at this first Session of Convocation after the inauguration of the National Health Service, this House desires to place on record its grateful appreciation of the generosity and kindness shown through many generations by members of the medical profession to the clergy and their families, as well as to countless other persons of small means, in times of sickness and need."

The Lower House of Convocation is a representative assembly of all the clergy of the Church of England in the southern two-thirds of England.

Wessex Rahere Club

The first annual dinner of the Wessex Rahere Club was held at the Royal Hotel, Bristol on Oct. 17. Dr. E. R. Cullinan attended from St. Batholomew's Hospital, and some thirty-six members were present under the chairmanship of Dr. G. D. Kersley. It was agreed that membership of the club should be open to all Bart's men resident in Somerset, Wiltshire, and Gloucestershire, with the possibility of extending the area later. Mr. C. E. Kindersley (Bath) was elected chairman and Mr A. Daunt Bateman (3, Circus, Bath) honorary secretary for the coming year. The 1949 dinner will be held in Bath on a Saturday in October. It is hoped that any Bart's men who are interested and have not yet been in touch with the club will notify their whereabouts to the honorary secretary so that they can be kept informed of future meetings.

Isotopes for Research

The Ministry of Supply states that radioactive isotopes have now been produced at Harwell for some months in the low-power pile to provide for the immediate needs of research workers. The production of the small pile is nearing its maximum and has recently been making about 120 samples a month, of which two-thirds have been for users outside the establishment. Among the isotopes of particular use to biological workers are Na^{24}, K^{42}, and Br^{82}, whose short half-lives preclude their import from America. Workers who wish to use isotopes are invited to discuss any unusual problem with the Isotope Information Officer, Atomic Energy Research Establishment, Harwell, near Didcot, Berks. Allocation of radioactive isotopes must be approved by the Isotope Allocation Committee (chairman, Sir John Cockcroft, F.R.S.). Radioactive isotopes may also be obtained from the U.S.A. and Canada, but requests must be sponsored by an appropriate authority such as the Medical Research Council. Inquiries should be addressed to the Secretary of the M.R.C., 38, Old Queen Street, London, S.W.1. The Ministry has purchased a quantity of N^{15} from the U.S.A. and allocated some of it to the M.R.C. The rest is available for distribution to workers whose research is sponsored by the appropriate body (for medicine, the M.R.C.). At present there is a shortage of mass spectrometers for assay, and the M.R.C., which has two instruments operating at the National Institute for Medical Research, Hampstead, is therefore prepared to do assay work and to advise in the preparation of samples from biological material.

Radioactive Elements for German Research

The Control Commission has decided that radioactive elements may be supplied for medical research in Germany. They will be provided from the atomic pile at Harwell, and their use will be demonstrated by a team from Harwell.

Ha'pence for Health

The National Association for the Prevention of Tuberculosis is an independent organization, receiving no money from the Government, whose aim is to help the tuberculous patient and to educate the public in the prevention of tuberculosis. In the last ten years it has raised about a quarter of a million pounds by selling attractive stick-on labels for Christmas letters and parcels. These labels, which have been given to the N.A.P.T. by the Canadian Tuberculosis Association, are now on sale again at 4s. a hundred from the Duchess of Portland, Chairman, N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1. Every halfpeny helps to keep alive the voluntary spirit which is so necessary to this work.

Nobel Prize for Work on D.D.T.

Dr. Paul Möller, of Basle, is to be awarded the Nobel Prize for Medicine for his discovery of the insecticidal properties of D.D.T. This substance was made in 1874, but it was first used as an insecticide in 1939 to check a plague of potato beetle in Switzerland. Dr. Möller was working in the laboratories of the J. R. Geigy Dyestuffs Company of Basle, which in 1942 drew the attention of the British Government to the usefulness of D.D.T. as an insecticide.

Vitamin C in Blackcurrants

The Ministry of Food announces that blackcurrant syrup and purée will again be available through retail chemists for children, invalids, and others in need of additional vitamin C. Children are those aged up to 18 holding green or blue ration books (RB2 or RB4). Owing to the high price of fruit this year, the maximum retail price of the syrup will be 2s. 10d. for a 13½-oz. bottle and of the purée 1s. 6d. for a 9½-oz. can. Both commodities will contain not less than 20 mg. of vitamin C per fluid ounce.

Mr. A. G. Timbrell Fisher

Mr. A. G. Timbrell Fisher has been elected to the Fellowship of the American College of Surgeons.

Dr. A. C. Norman

The King of Iraq has conferred the decoration of Insignia of the Third Class (Civil Division) of the Order of Al Rafidain upon Alfred Clarence Norman, C.B.E., M.D., in recognition of valuable services rendered by him as Director of the *X*-ray Institute at the Royal College of Medicine, Bagdad.

Medical Golf

The following are the results of the competitions at the autumn meeting of the Medical Golfing Society held at Royal St. Georges: Lindsay-Rea Cup, Dr. C. Carron Brown (5), 3 up; Canny Ryall Cup, Dr. G. Armitage (5), 72; Veterans Cup, Dr. D. Craig (12), 74; Milsom Rees Cup, Dr. A. Galletly (4).

The autumn meeting of the London Irish Medical Golfing Society was held at Aldeburgh. The results are as follows: O'Malley Cup, Dr. R. J. Sandys (15), 1 down; Lett Cup (foursome), Dr. T. J. Kelleher and Dr. T. Murphy, 1 down; Canny Ryall Cup, Dr. G. Purcell (12), 70; Cahill Trophy, Dr. S. C. Morrow (13); Mannix Cup, Dr. S. C. Morrow (13); Veterans Prize, Dr. J. J. Cremin (8), 79.

The London Irish Ladies Medical Golfing Society have completed a successful year with a meeting at Beaconsfield. The following were the winners of the competitions: Scratch Prize, Mrs. E. McGrath (19), 97; Canny Ryall Cup, Mrs. K. Cowles (26), 80; Foursomes, Mrs. E. McGrath and Mrs. K. Nolan (all square). The captaincy has been held by Mrs. G. Walters, and the secretarial duties have been carried out by Mrs. R. Lindsay-Rea. The annual general meeting is being held to-day, Nov. 5, at 82, Harley Street, London, W.1.

Wills

Dr. Legh Richmond Herbert Peter Marshall, of Walkerburn, Peebles-shire, left £31,090. Dr. Alfred Milne Gossage, of Chalfont St. Giles, Bucks, late consulting physician to the Westminster Hospital and of the Princess Elizabeth of York Hospital for Children, left £17,236. Mr. Henry Secker Walker, of Bradford-on-Avon, Wilts, left £114,937. Dr. William James Deacon Inness, of Horwood, Devon, late Director of Medical Services, West African Medical Staff, left £4,329.

COMING EVENTS

London Chest Hospital

A course of lectures and demonstrations will be given at the London Chest Hospital (Victoria Park, E.) on Fridays, at 5 p.m., from Nov. 5 to Dec. 17, 1948, and from Jan. 7 to March 25, 1949. Admission is by ticket only. The fee is £3 3s., except in the case of serving and demobilized members of H.M. and Allied Forces. Applications should be addressed to the dean of the hospital. Details of the lectures will be published in the diary column of the *Journal* week by week.

Maudsley Lecture

The twenty-third Maudsley Lecture will be delivered by Mr. Claud Mullins before the Royal Medico-Psychological Association at 26, Portland Place, London, W., on Friday, Nov. 12, at 2.15 p.m. His subject is "Psychiatry in the Criminal Courts." Psychiatrists and other medical practitioners, psychologists and members of the legal profession, teachers and students, and all interested are invited to attend the lecture. Admission is without ticket.

S.E. Metropolitan Regional Tuberculosis Society

The inaugural meeting of the South East Metropolitan Regional Tuberculosis Society will be held at the County Hospital, Sevenoaks Road, Orpington, Kent, on Nov. 13 at 10.30 for 11 a.m. The Constitution of the Society will be discussed and approved and the assembly will be addressed by the Senior Administrative Medical Officer of the Region, Brigadier H. L. Glyn Hughes. All interested practitioners in the Region, and particularly those engaged in chest work, are invited to attend.

Public Health Congress

The provisional programme of the Public Health and Municipal Engineering Congress and Exhibition, to be held at Olympia, London, from Nov. 15 to 20, has been issued. The programme is not yet complete, but 21 sessions have been arranged under the auspices of the leading professional institutes and associations, and 26 papers will be read, the subjects, to which additions will be made, including hospital administration in the National Health Service, mental health services, refuse storage, sewage, rural water supplies, water supply gathering grounds, district heating, communal health facilities on housing estates, housing of old people, plumbing research, quarrying and highway engineering, planning of a new town, park organization and equipment, and health visitors' work. The Exhibition and Congress are being held under the patronage of the King and the presidency of the Minister of Health, and the Ministries of Health and Transport are both represented on the organizing council, the chairman of which is Sir Roger G. Hetherington. The joint honorary secretaries are Mr. G. P. Warner Terry and Mr. C. W. Scott-Giles, and the Congress address is 84, Eccleston Square, London, S.W.1. Contributions of particular interest to the medical profession include papers by Sir Ernest Rock Carling on "The Provision of Homes for Old People" on Nov. 15, at 3 p.m.; by Mr. George Watts on "Hospital Administration in the National Health Service" on Nov. 16, at 10.30 a.m.; by Dr. Rees Thomas on "Mental Health Services" on Nov. 17, at 10.30 a.m.; by Mr. A. R. Kerrell-Vaughan on "The Provision of Communal Health Facilities on Housing Estates" on Nov. 19, at 10.30 a.m.; and by Miss B. Townsend on "The Health Visitor's Place in the Health Team" and Miss E. C. Jackson on "Day Nurseries, their Uses and Abuses" on Nov. 20, at 3 p.m.

Films on the "Neuraxis"

A joint meeting of the Scientific Film Association and the Royal Society of Medicine will be held at 1, Wimpole Street, London, W., on Monday, Nov. 15, at 8 p.m., when Professor Pedro Belou, professor of anatomy at the Faculty of Medical Sciences, Buenos Aires, will show his films on the "Neuraxis." Fellows of the Society and visitors introduced by Fellows will be welcome.

SOCIETIES AND LECTURES

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—Nov. 8, 8 p.m. Pathological meetings.

UNIVERSITY COLLEGE, Gower Street, W.C.—Nov. 8, 4.45 p.m. "*The Electron Microscope and its Biological Applications*," by Dr. E. M. Crook, M.Sc., Ph.D.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—Nov. 8, 5.30 p.m. "*Pyelonephritis and Renal Suppuration.*" Clinico-pathological meeting.

Tuesday

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 47, Queen's Gate Terrace, London, S.W., Nov. 9, 7 for 7.30 p.m. "*The Value of Chironody in Foot Disabilities.*" Discussion to be opened by Mr. J. H. Hanby, F.I.S.Ch.

GLASGOW UNIVERSITY.—Nov. 9, 4.30 p.m., "*The Evolution of Medical Education in Scotland*," by Dr. Douglas Guthrie.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Nov. 9, 5 p.m. "*Scars*," by Dr. H. Corsi.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330-2, Gray's Inn Road, London, W.C.—Nov. 9, 11.30 a.m., "*The Physical Principles of Audiometry and Hearing Aids (II)*," by Dr. T. S. Littler; 2.15 p.m., "*The Respiratory Tract in Infectious Diseases*," by Dr. E. H. R. Harries.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 9, 11 a.m., "*Latent Syphilis*," by Dr. W. N. Mascall; at St. Peter's Hospital, Henrietta Street, London, W.C., Nov. 9, 5 p.m., "*Calculous Disease of the Bladder and Urethra*," by Mr. F. R. Kilpatrick.

Wednesday

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 10, 11 a.m., "*Manifestations of Tertiary Syphilis*," by Dr. A. H. Harkness; at St. Peter's Hospital, Henrietta Street, London, W.C., Nov. 10, 5 p.m., "*Injuries of the Bladder: Foreign Bodies in the Bladder*," by Mr. J. G. Sandrey.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—Nov. 10, 5 p.m. "*The Clinical Use of the Antihistamine Drugs*," Finlayson Memorial Lecture by Professor D. M. Dunlop.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—Nov. 10, 3.30 p.m. "*Placing the Impaired Worker in Industry*," by N. L. Lloyd.

ROYAL SANITARY INSTITUTE, 90, Buckingham Palace Road, London, S.W.—Nov. 10, 2.30 p.m. "*Science in the Imported Meat Industry*," Benjamin Ward Richardson Lecture by Dr. E. H. Callow, Ph.D., and Dr. M. Ingram, Ph.D.

Thursday

EDINBURGH ROYAL INFIRMARY.—Nov. 11, 5 p.m. "*The Diagnosis and Treatment of Depression*," Honyman Gillespie Lecture by Dr. T. A. H. Munro.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Nov. 11, 5 p.m. "*Pruritus*," by Dr. L. Forman.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 11, 11 a.m., "*Cardiovascular Syphilis*," by Dr. E. G. B. Calvert; 5 p.m., "*Marion's Disease (Bladder Neck Obstruction) and Vesical Diverticula*," by Mr. W. K. Irwin.

PLANNING FORUM.—At Planning Centre Hall, 28, King Street, Covent Garden, London, W.C., Nov. 11, 6.15 p.m. "*Population and Emigration*," discussion to be opened by Professor Brinley Thomas, Ph.D., and Mr. R. J. Goodman.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—Nov. 11, 5 p.m. "*Proctology Throughout the Ages*," Bradshaw Lecture by Mr. L. E. C. Norbury.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—Nov. 11, 4.30 p.m. "*Neurology and Psychiatry*." Lecture-demonstration by Dr. Desmond Curran.

Friday

LONDON CHEST HOSPITAL, Victoria Park, E.—Nov. 12, 5 p.m. "*Acute Respiratory Infections*," by Dr. R. Sleigh Johnson.

ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, London, W.C., Nov. 12, 5.15 p.m. "*Morality and the Social Sciences*," by J. A. Passmore, M.A.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—Nov. 12, 8 p.m. "*Exophthalmos*," by Mr. D. S. Alexander.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.—At 26, Portland Place, London, W., Nov. 12, 2.15 p.m. "*Psychiatry in the Criminal Courts*," Maudsley Lecture by Mr. Claud Mullins.

SELLY OAK HOSPITAL MEDICAL SOCIETY, Birmingham.—Nov. 12, 8 p.m. "*Hypoglycaemia*," by Professor Henry Cohen.

WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At Miller Hospital, Greenwich High Road, London, S.E., Nov. 12, 8.30 p.m. "*Treatment of Skin Conditions in General Practice*," by Dr. W. G. Tillman.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Holmes.—On Oct. 25, 1948, at Edgware, the wife of Mr. Stanley Willson Holmes, a son.

Jones.—On Oct. 29, 1948, at Gainsborough House, Willows Avenue, Morden, to Evelyne, wife of Dr. G. Lewis Jones, a daughter—Margaret Lynne.

Kennedy.—On Oct. 16, 1948, at Clifton Nursing Home, Whitchurch, to Patricia (ex-Q.A.I.M.N.S/R), wife of Dr. D. B. Kennedy, a son.

Logie.—On Oct. 26, 1948, at Rubislaw Nursing Home, Aberdeen, to Kathleen (née Neill), wife of Norman J. Logie, F.R.C.S., 4, Albyn Terrace, Aberdeen, a daughter.

McMillan.—On Oct. 23, 1948, at Carlisle Maternity Hospital, to Monica Corlette (née Brown), wife of Dr. R. L. McMillan, a daughter.

Murray.—On Oct. 17, 1948, at Regent's Park Nursing Home, to Jean, wife of Dr. Neville Murray, of 101, Barons Keep, Barons Court, London, W., a son—Stephen Francis.

Nicholson.—On Oct. 30, 1948, at Harrogate, to Frances (née Burdon-Cooper, B.Sc.), wife of B. Clive Nicholson, M.D., M.R.C.P., a son.

Parry.—On Oct. 21, 1948, at Cardiff, to Joan, wife of John N. M. Parry, M.B., B.S., F.R.C.S., a daughter.

Podolier.—On Oct. 4, 1948, to Diana (née Myott), M.B., B.S., wife of Paul Podolier of 8, Graham Road, Purley, a daughter—Janet Frederica.

Steele.—On Oct. 24, 1948, at Vaynor House, Welsh Street, Chepstow, to Phyllis, wife of Captain D. E. Steele, R.A.M.C., a daughter—Hilary Ann, a sister for Robert.

MARRIAGE

Poolman—Lansell.—On Oct. 28, 1948, at Melbourne, Australia, John, only son of the late Ernest Poolman and Mrs. Poolman, of Amesbury House, South Yarra, Melbourne, to Deborah Lansell, fourth daughter of Colonel A. J. and Mrs. Staughton, of "Keayang," Terang, Victoria, Australia.

DEATHS

Brind.—On Oct. 23, 1948, at Garran Haven, Cornwall, Harry Hanslow Brind, M.R.C.S., L.R.C.P., D.P.H.

Grossart.—On Oct. 23, 1948, Robert Kerr Grossart, M.B., Ch.B.Glas., D.P.M.

Paterson.—On Oct. 22, 1948, at Brookfield House, Millbrook, near Plymouth, Alexander Cowie Paterson, M.B., Ch.B., D.P.H.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Hodgkin's Disease

Q.—*What is the latest treatment of Hodgkin's disease? What are the results of treatment with nitrogen mustard? Is irradiation still the most efficient treatment?*

A.—It is optimistic to regard any treatment for Hodgkin's disease as efficient. Irradiation remains the standby, and it will usually cause the enlarged lymph nodes to shrink, though most patients finally become "radio-resistant." The nitrogen mustards, especially methyl-*bis*-(beta-chloro-ethyl)-amine hydrochloride, have been used recently, and in many instances will cause a temporary remission in the disease. This substance does not cure Hodgkin's disease, and in the early stages radiotherapy is to be preferred. Nitrogen mustard is often effective in relieving—albeit temporarily—the symptoms of the generalized stage, such as fever, cachexia, prostration, pruritus, and the pain of skeletal infiltrations. Some patients whose disease has become resistant to irradiation are improved by a course of this drug.

Stilboestrol in Dysmenorrhoea

Q.—*Is there any danger in treating severe dysmenorrhoea with stilboestrol indefinitely? The case I have in mind is a patient of 22 who has been having 1 mg. stilboestrol daily for the first ten days of the menstrual cycle. Recently she had a dilatation and curettage, but this failed to relieve the dysmenorrhoea, and the administration of stilboestrol was recommenced. If prolonged treatment with stilboestrol is contraindicated, what alternative is recommended?*

A.—If a psychological effect is excluded—as it can be by substituting inert tablets for the stilboestrol—oestrogens probably relieve dysmenorrhoea only when they are given during the first half of the cycle in a dose sufficiently large to suppress ovulation. Their effect, therefore, is limited to the cycle during which they are administered. Although it is not possible to produce concrete evidence, it is reasonable to suppose that prolonged and deliberate disturbance of the ovarian cycle in this way is potentially, if not actually, harmful in a young woman. The writer would therefore advise against sustained oestrogen therapy for dysmenorrhoea. Indeed, all forms of hormone therapy generally give unsatisfactory permanent results in this condition.

The treatment depends very much on the cause of the pain. Have psychogenic and environmental factors been excluded? Have active physical exercises been tried? What type of dysmenorrhoea is present: is it congestive, or is it of the spasmodic variety? If the latter, antispasmodics might be of some value, but failing that a second and more thorough dilatation of the cervix might be carried out. Hysterosalpingography to exclude malformation of the uterus might be useful. If all else fails and the pain is so severe as to be incapacitating, injection of the pelvic plexus with alcohol or presacral neurectomy should be considered.

Sterilization by Steam

Q.—*What is the correct pressure for steam-sterilizing gowns, dressings, and gloves? A salesman tells me that 10 lb. (4.5 kg.) for 35 minutes is absolutely safe, and is anxious to sell me a sterilizer to operate at this pressure.*

A.—The deciding factor in sterilization is not pressure but temperature. The temperature of pure steam at 10 lb. pressure is 115° C., and this is barely adequate for absolute sterilization. If steam under this pressure is admitted to a closed vessel containing air with no arrangement for displacing the latter, the temperature reached will be only 90° C. If half the air is discharged it will be 105° C. The answer therefore depends on the arrangements for air discharge: only if this is complete, the air being blown out by steam before closing and allowing the pressure to rise, could this sterilizer be considered efficient.

Physiology of Hearing

Q.—*I have been unable so far to find an authority who can give me any information about the specific gravity of the fluids in the cochlea and their viscosity, especially in diseased ears. I would also like references to information about theories of hearing.*

A.—The perilymph has the same chemicophysical properties as cerebrospinal fluid. No record of analysis of endolymphatic fluid has been found. Modern views on the physiology of hearing may be culled from Stevens, S. S., and Davis, H. (1938), *Hearing: Its Psychology and Physiology*, John Wiley and Sons, New York; Fowler, E. P. (1937), *Laryngoscope*, **47**, 289.

Congenital Cystic Disease of Pancreas

Q.—*A child aged 4 suffers from congenital cystic disease of the pancreas. He secretes no pancreatic juice at all. There is also a severe bronchial cough. Pancreatin is given regularly. Has this treatment been "proved" or not? What is the prognosis? What can be done about the cough?*

A.—The prognosis at the age of 4 years depends largely on whether the pulmonary complication can be kept under control. If the cough is troublesome it would be advisable to try a course of aerosol penicillin inhalations, 20,000 units in 2 ml. normal saline three to five times a day for a week. If this is effective, the same dose night and morning might be continued for another three weeks or according to progress. The invading organism is usually *Staphylococcus aureus*, but if not sensitive to penicillin then a sulphonamide or streptomycin might be tried. As there is a danger of converting sensitive organisms to resistant ones it is advisable to stop aerosol treatment during the better periods of the respiratory condition.

Pancreatin improves the stools and seems to aid absorption of food from the gut. Anderson recommends its use, though May has cast doubt upon its clinical efficacy. Anderson considers diet and pancreatin given early in the disease help to prevent pulmonary complications. Usually as the child grows older improvement is observed, and so far cases have been followed up to fifteen years.

Hartmann's Solution

Q.—*The Ringer-lactate (Hartman's) solution formerly used for intravenous therapy in infants in this hospital was made up by adding an ampoule of concentrated solution to 480 ml. of sterile distilled water and then adding the required amount of glucose solution to make a 5% solution. Our still gives slightly acid water, and a small amount of sodium hydroxide was added before autoclaving. The final solution had a pH of about 8.0 (phenol red). Recently we have altered the method and the glucose is added to the water before autoclaving. Because of this we are unable to add the caustic soda, as it tends to caramelize the glucose. The final solution now has a pH of 6.2; will this make any difference, or will the lactate be sufficient to buffer this in the blood? Can this solution still be used for the treatment of dehydration whether accompanied by acidosis or alkalosis?*

A.—The slight acidity of the Hartmann solution will not have any ill effect, and once the lactate is oxidized in the body an ample excess of alkali will be available. It is therefore useful for correcting acidosis, but in alkalosis Hartmann's solution should not be used; a simple glucose–saline solution is preferable.

Injection Treatment of Hydrocele

Q.—*Are good results obtainable in the treatment of hydrocele by injection with quinine and urethane, and is this treatment painless? How does the result compare with operation in a patient aged 56?*

A.—The injection treatment of hydrocele—carefully carried out—will certainly produce good results, but should always be considered a second-best treatment in comparison with operation. This is because incomplete results due to loculation rather than obliteration of the hydrocele sac are by no means uncommon. It would be unwise to promise that the treatment is painless. Reactions vary greatly from patient to patient, and are seldom completely absent. If the patient of 56 is otherwise fit he is much better advised to have an operation.

NOTES AND COMMENTS

Treatment of "Tennis Elbow."—Dr. JAMES CYRIAX (London, W.) writes: Surely the answer to the question on how to treat a "tennis elbow" (Oct. 9, p. 699) is not very helpful. It merely lists a number of treatments to be tried one after the other. In fact, the answer is simple. There are three varieties of "tennis elbow." In the commonest (90%) the lesion lies at the lateral humeral epicondyle. For this variety no treatment known to me surpasses Mills's manipulation, which even when carried out by our students of physiotherapy at St. Thomas's Hospital fully relieves three-quarters of all cases within a month. When the lesion lies at the musculo-tendinous junction, deep massage there is usually curative in three weeks. When the lesion lies in the bellies of the extensor muscles, two or three infiltrations with procaine bring about lasting recovery.

Difficult Delivery.—Dr. WALTER MCMANN (Danville, Va., U.S.A.) writes: The answer to the question on this subject (Sept. 18, p. 583) seems to evade the question. A baby can present itself by the vertex, occipito-anterior, and still be delivered with difficulty. The trouble is that asynclitism, which is present during the descent of the foetal head, persists after rotation. The sagittal suture, instead of being in the midline, is several degrees to the side, usually left. The occiput is still anterior. Proper application of the forceps means putting them on at an angle so that the sagittal suture is perpendicular to the shank of the forceps. The handles are then brought to the midline by a sideways movement. While an assistant presses just above the symphysis to the opposite side (Willett's forceps could be used to hold the head in place) the forceps are checked and reapplied if necessary. Extraction follows. Of course a difficult delivery can also be occasioned by the sagittal suture being in the midline and the head deflexed, but from the description given of the forceps marks by the questioner I think this is not the difficulty which has been encountered.

Transplantation of Ureter into Appendix.—Mr. A. H. MORLEY (Surgical Specialist, Tanganyika Territory) writes from Dar-es-Salaam: In your issue of Aug. 7 (p. 321) in reply to a question from the Congo on transplantation of the ureter into the appendix you state that the risks of reflux infection are appreciably increased by reason of the more fluid contents of the caecum as compared with the usual site in the pelvic colon. But is this really so? At the site of anastomosis, wherever it may be, there must be a pool of mixed urine and faeces, and the lower down this is the more highly infected it will be. I had this brought home to me vividly some years ago in a case at the Sewa Haji Hospital. These very large vesico-vaginal fistulae are common in this part of Africa from difficult labour in immature girls in the bush, and when as frequently happens there is an extensive recto-vaginal fistula as well there is a problem indeed. In this case I made the usual examination under an anaesthetic and satisfied myself that the vesico-vaginal fistula was irreparable by me and that there was no recto-vaginal fistula. I then transplanted the ureters into the colon and was dismayed to find that her condition was now worse in that she now leaked both urine *and* faeces per vaginam. Further examination then showed that she had a very small high recto-vaginal fistula in the posterior fornix, the lumen of which was certainly no greater than that of the ureter and through which a mixture of faeces and urine was pouring.

I have utilized the appendix on one occasion for a unilateral transplant for an operation injury to the right ureter. In this case it seemed to be of advantage in that the patient passed apparently normal motions instead of the two or three watery motions daily which are the usual result of ureter transplants into the colon. It would seem that it can matter little from the point of view of the danger of reflux infection where the anastomosis is made, and that the main consideration in the choice of site should be the ease and safety with which the operation can be performed; from this point of view the appendix may have something to recommend it.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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